U.S. Army. Far East Command.
Military Intelligence Section

3460

25859

LOCUS OF IMPACTION OF PARTICULATES

524898

15 DECEMBER 48

REPORT BY

GHQ TECHNICAL INTELLIGENCE DETACHMENT

G31/M-55

GENERAL HEADQUARTERS
FAR EAST COMMAND
MILITARY INTELLIGENCE SECTION
Technical Intelligence Detachment

KI/mlm

APO 500
15 Dec 48

SUBJECT: Locus of Impaction of Particulates

TO: Director, Department of the Army (Strategic) Intelligence Division, G-2, GHQ, FEC, APO 500

1. AUTHORITY: G-2, GHQ IOM, Chief, Target Branch to C.O., TID Thru: Director, MIS Div, subject: "Locus of Impaction of Particulates," dtd 9 Mar 48

2. REFERENCES:

a. Ltr, DA, GSUSA, Intell Div, Washington 25, D.C., file ID 350.05, subject: "Locus of Impaction of Particulates," dtd 26 Feb 48

b. Rpt, TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 16 Apr 48

3. PURPOSE: To secure additional information on the locus of impaction of particulates (living organisms as well as inorganic particles) in the respiratory tract

4. DETAILS OF INVESTIGATION: Noted Japanese scientists and medical authorities on industrial hygiene and related field at private and public institutions were visited and interviewed by an investigator of this unit on the subject: "Locus of Impaction of Particulates in the Respiratory Tract," as follows:

Personnel Interviewed	Institution and Address	Date of Visit
Dr. Susumu ISHINISHI and Dr. Goro NIWA	MITSUI SANGYO IGAKU KENKYJO (Mitsui Medical Institute for Industry); Fukuoka-ken Kaho-gun, Inatsuka-machi, Kamo, 55	6 May 48
Dr. Namio SARUTA and Dr. Maseichi ISHIZAWA	Department of Hygiene, Faculty of Medicine, Kyushu University; Fukuoka-ken, Fukuoka-shi, Katakasu, 1276	7 May 48
Professor Tando MISAO	Department of Anatomy, Faculty of Medicine, Kyushu University; Fukuoka-ken, Fukuoka-shi, Katakasu, 1276	9 May 48

Assistant Professor Masashichi NISHIO	Department of Hygiene, Faculty of Medicine, Kyoto University; Kyoto-fu, Kyoto-shi, Sakyo-ku	11 May 48
Dr. Kesao KOBAYASHI	FURUKAWA DENKI K.K., ASHIO KOZAN BYOIN (Furukawa Electric Co., Ltd., Ashio Mine Hospital); Tochigi-ken, Kamitsuga-gun, Ashio-machi, 5277	15 May 48
Dr. Kaneyoshi AKAZAKI	Niigata Medical College; Niigata-ken, Niigata-shi, Suido-cho, 2-chome, 808	19 May 48
Dr. Ugoro KOINUMA	Department of Hygiene, Faculty of Medicine, Nagoya University; Aichi-ken, Nagoya-shi	Jun 48
Dr. Tsuneo HASEGAWA	Research Laboratory of Mitsubishi Mining Co., Ltd., Saitama-ken, Omiya-shi, Kitabukuro-cho, 16	Aug 48

The research results, both published and unpublished reports to which frequent references were made by the Japanese scientists, have been secured, translated, and condensed into abstract reports hereto attached as 18 inclosures in fullfilment of the requirements for the investigation. Other publications of similar contents are referred to the original journal by citing the references. Among the scientists interviewed, Dr. Kaneyoshi AKAZAKI was able to furnish a considerable amount of information pertaining to the studies on pneumoconiosis in Japan.

5. SUMMARY OF INFORMATION:

a. In June 1940, Dr. Susumu ISHINISHI, Director of the Mitsui Medical Institute for Industry, and his assistants commenced studies on the influence of dust particles used in the coal mines upon the human body by using rabbits as experimental animals under intensified experimental conditions over a prolonged period of time. Limestone dust, which is used as anti-explosion agent in the coal mines, was circulated in the "ROKEN" Type dust inhalation apparatus under similar intensity as that observed in the mines for irregular daily inhalation periods extending over 25 days duration. In this experiment, no deposition of dust particles was observed in the lungs of the rabbits probably due to the presence of a large percentage of calcium carbonate (40.85% CO_2 and 51.00% CaO) and a low percentage of silica (4.24% SiO_2). Nevertheless, different pathological changes were observed in the respiratory organs, such as congestion, dropsy, hemorrhage, atelectase in the lungs, epithelium ablution in the trachea, and epithelium necrosis in the larynx. The results of the experiment were published in

the abstract form in the Igaku to Seibutsugaku, 11, No. 4, 235-239 (1947) and the complete unpublished report entitled "Injurious Effect of Rock Powder Used in Coal Mines upon the Respiratory Organs, Part I Experiment with "SS" Rock," by Doctors Shiko TAKEYA and Susumu ISHINISHI was abstracted and attached as Inclosure 1.

In the second experiment conducted from July 1940 with rabbits and guinea pigs, Cottrell dust was circulated in the dust inhalation apparatus under assimilated conditions comparable to those in the mines. The experiment was conducted for a period of 1100 days for the rabbits with the maximum exposed inhalation time of 6,284 hours and 262 days duration for the guinea pigs with 1,698 hours of exposure to dust inhalation. In all the test animals acute or sub-acute laryngitis and trachitis were observed. The deposition of the dust particles in the lymphatic glands of the pulmonary hilus was observed sooner in the guinea pigs than in the rabbits. The deposition grew steadily in size and proliferation occurred as the time progressed. The heart, spleen, and liver underwent pathological changes but not to any marked degree. The results are summarized in the unpublished report "The Influence of the Rock Powders Used in Coal Mines upon the Human Body" by Doctors Tadatoshi MIYAZAKI and Goro NIWA, Inclosure 2.

In both of the experiments, neither could the concentration of the dust particles blown into the dust inhalation apparatus be quantitatively denoted nor the same humidity existing in the mines maintained. No study was made on the distribution of the dust particles by size in the respiratory tract or the degree of exhalation of the dust particles from the respiratory tract by the tracheal ciliary motion. It was observed that the dust particles smaller than 300 mesh were ingested by the dust cells and found in the pulmonary alveoli. Since the termination of the experiment in April 1944, no further animal experimentation has been conducted due to financial difficulties in maintaining the experimental animals.

According to Dr. ISHINISHI, similar projects were carried out by Dr. Kentaro HIYEDA (present status unknown), formerly Professor of Pathology at the Manshu Medical College, Manchuria, and his assistants, Atsunori OSHIMA and Hiroshi NOGAMI, on the study of silicosis. Two well known papers have been published entitled "Myocardial Lesion by the Continual Inhalation of Silica Dust" in the Journal of the Manshu Medical College, 37, No. 6, 1373-1410 (1942) and ibid, 35, No. 4, 551-562 (1941).

b. Dr. Namio SARUTA, Professor of Hygiene, Kyushu University Medical School has made an extensive statistical studies on the atmospheric gas concentration in Japanese industrial plants, but has not conducted studies on the mechanism of gas absorption into the blood system through the respiratory system. Dr. SARUTA furnished information on the research project conducted by Dr. Hideichi ODA (present location unknown) about 1941 at this laboratory concerning the experimental studies on the influence of textile fibers on the lungs of rabbits and its relationship to the development of tuberculosis. In Dr. ODA's experiment with young rabbits, various cotton, wool, and staple fibers were circulated in a dust inhalation apparatus over a period of 10 to 120 days. Upon pathological investigation, the fibers were found to be filtrated deep into the alveoli by normal breathing and caused vicarious emphysema, but no proliferation of the connective tissues was observed. His conclusions indicated evidences that lesion of the lungs caused by the continuous inhalation of the dust fibers, even in slight and mild degrees, was proved to be a powerful inducement to the development of tuberculosis. The results of Dr. ODA's research, entitled "Experimental Studies on the Influence of Textile Fibers on the Lungs of the Rabbits and the Development of Tuberculosis," was published in the Fukuoka Medical Journal (Japan), 36, 511-542 (1943) and an abstract of the paper is attached to this report as Inclosure 3.

Dr. Masaichi ISHIZAWA, Department of Hygiene, Kyushu University Medical School, conducted experiments during 1943-1944 under the direction of Dr. Itsuo KURODA, who was then Head of the Department of Hygiene, on the correlation between silicosis and pulmonary tuberculosis by using albino rats. Dr. KURODA is presently practicing private medicine, after retiring from the Department of Hygiene, at Fukuoka-ken, Tobata-shi, Shimizu-cho, 4-chome. The experiment was divided into 5 different groups and conducted for a duration of 16 weeks. Different pathological changes were brought about with prolonged inhalation of silica dust and more so if subcutaneous injection of tubercule bacilli was made. When silica dusts (93.12% and 89.96% SiO_2) were inhaled 1 hour/day for 57 inhalations during 16 weeks, the pulmonary alveolar septa were partially infiltrated with diffusive round cells and proliferated; the pulmonary alveoli were slightly dilated, disintegrated or fused with one another to form networks; the bronchial epithelial cells were proliferated to a pronounced degree or partially desquamated; pronounced engorgement of the capillary blood vessels of the pulmonary alveolar septa and hemorrhage of the interstitial substances were often observed. After subcutaneous injection of tubercule bacilli was made, numerous small hemorrhage blotches as well as whitish grey tubercules of millet size were sporadically observed. Details of the experiment are given in Dr. KURODA's unpublished report entitled "Experimental Study on the Correlation between Silicosis and Pulmonary Tuberculosis," which is attached to this report as Inclosure 4.

Dr Tando MISAO, Professor of Anatomy, Kyushu University Medical School, is an authority on dengue fever, influenza, and encephalitis japonica (encephalitis B) viruses. According to Dr. MISAO, no research has been conducted in Japan on the lodgment of viruses in the respiratory tract. However, it is possible for the viruses to adhere to fine dust particles (smaller than 1 μ diameter) and be inhaled into the respiratory tract either through the nasal passage or through the mouth during normal inhalation.

c. Assistant Professor Masashichi NISHIO, Department of Hygiene, Kyoto University Medical School, disclosed that no research projects on pneumoconiosis has been conducted since the commencement of World War II at this laboratory. Prior to the war, numerous projects were carried out on the discharge process and the expelling velocity of foreign particles by ciliary action of the trachea by the following research workers: Doctors Masanobu SAITO (presently practicing medicine somewhere in Osaka), Seisaburo NAGATANI (present whereabouts unknown), Kazuo TAKEUCHI (private practice, present location unknown), and Minoru YANAGIBASHI (deceased). The important published papers have been abstracted and attached to this report as follows:

Inclosure No.	Titles of the Experiment	Authors	Publication
5	"Discharging Process and the Expelling Velocity of Inhaled Dust in the Trachea"	Seisaburo NAGATANI	National Hygiene (Japan), 7, 436-454 (1932)
6	"Influences of Various Physico-chemical Condition upon Dust Expelling Function of Trachea"	Seisaburo NAGATANI	ibid, 7, 645-71? (1932)
7	Comparative Study of Dust Expelling Velocity of Trachea of Various Species of Animals"	Masanobu SAITO	ibid, 9, 395-406 (1934)
8	"Comparative Study of Dust Expelling Velocity in Trachea of Animals of Various Ages"	Masanobu SAITO	ibid, 9, 407-414 (1934)
9	"Pathological Changes of the Mucous Membrane of Trachea by Continuous Inhalation of Various Poisonous Gases and Their Relationship with Foreign Body Expulsion Action"	Kazuo TAKEUCHI and Minoru YANAGIBASHI	ibid, 11, 1447-1462 (1935)

The measurement of the dust expelling velocity of different animals was made by Dr. S. NAGATANI with respect to the shape, hardness, and specific gravity of dust particles, such as cork, charcoal, coal, sand, glass, zinc, iron, brass, copper, and lead powders. The results obtained (refer to Inclosure 5) indicate that the velocity of the dust particles depends upon the surface of the trachea from which the samples were taken and does not depend upon the shape, hardness, and specific gravity of the dust particles. Dr. NAGATANI has conducted a series of studies on the influence of various physico-chemical conditions, such as chemicals, drugs, narcotics, etc., upon the dust expelling velocity of the trachea by using 0.074-0.088 mm diameter charcoal dust as the foreign substance. The effects are varying under different conditions and the detail results are tabulated in Inclosures 6 and 7.

Dr. M. SAITO has found that the dust expelling velocity of extracted trachea varies with the different species of animals and the infant animals possess slower rate of dust expelling velocity than adult animals (refer to Inclosure 8). It has been ascertained by Dr. M. SAITO that the maximum size of the dust particles, which can be expelled, varies with the different animal species. Thus, the facts indicate that dust particles , which are too large to be expelled, will never enter the trachea in the normal inhalation period.

Doctors K. TAKEUCHI and M. YANAGIBASHI have studied the foreign body expulsion speed and the state of recovery after inhaling poisonous gases (sulfur dioxide, hydrogen sulfide, and carbon disulfide) for one hour a day for a period of 30 days were determined by using rabbits. The formation of vesicles and cerebral vesicles are due to the degeneration and collapse of the epithelial cells of the trachea by the chemical stimulation of the poisonous gases. The results are published in the National Hygiene (Japan), 11, 1447-1462 (1935), Inclosure 9.

According to Assistant Professor NISHIO, Professor Shozo TODA planned to investigate experimentally, prior to his retirement in 1945, the problem of droplet infection with special emphasis placed upon the relationship between the intensity of exhalation and the degree of infection by using pneumonia bacteria on rabbits. Unfortunately, the bacteria died while the experiment was in the preparatory stage. Thus, the project was abandoned and no experimental data were secured.

d. Dr. Kesao KOBAYASHI, Director of the Ashio Mine Hospital of Furukawa Electric Co., Ltd., Tochigi-ken, Kamisuga-gun, Ashio-machi, 5277, has conducted extensive studies on the progress of silicosis among the mine workers by means of X-ray photographs. Particular attention has been paid to the relation between the dust particles inhaled and the development of silicosis, but no study was made on the amount of dust particles retained in the alveoli or the mechanism by which the dust cells containing the ingested dust particles migrated to the different parts of the lungs. The post mortem examination of the lungs of silicosis patients disclosed that the extent of the silica deposition was large, but no measurement of the size or its distribution at different points in the lungs was made. Dr. K. KOBAYASHI has developed a portable dust collecting apparatus, the ASHIO Konimeter (a modified Zeiss Konimeter), by which dust samples from the mine are secured and measured under the microscope. The size distribution of the silica dust particles (47-57% free silica) of the Ashio Mine was found to be as follows: 0.6% $>10\,\mu$, 1.4% 5-10 μ, 25.4% 1-5 μ, and 72.6% $<1\,\mu$. The minute dust particles, $<1\,\mu$, can reach the deepest part of the lungs, while the larger sizes are unable to reach or enter passage-ways smaller than the diameter of the dust particles. A certain amount of the inhaled dust particles are removed by the ciliary action of the trachea and by coughing caused by irritation of dust particles. Thus, the percentage of the dust particles retained in the respiratory tract remains unknown. A similar experiment to Dr. KOBAYASHI's has been conducted by Dr. Kyuji SHIRAKAWA, Chief of the Yubari Mine Hospital of Hokkaido Coal Mine and Steamship Co., Ltd., who has studied anthracosis and published the results in a report entitled "Anthracosis and Tuberculosis," Kekkaku, 9, No. 2, 75-407 (1931).

e. In 1935, Professor Kaneyoshi AKAZAKI, Department of Pathology, Niigata Medical College, commenced studies on pneumoconiosis under Professor SCHOFF at Freidburg University, Germany, for a period of one year. Upon his return to Japan, Professor AKAZAKI with the assistance of different medical researchers at the Niigata Medical College continued his research on pneumoconiosis. A series of animal experimentation was carried out as well as correlating the findings with careful post mortem examination of the miners afflicted with silicosis. The findings of the experiments conducted by Dr. AKAZAKI and his assistants were referred to the published papers and explaind in detail as follows:

(1) Seiichiro KIRYU, a student of Professor AKAZAKI, conducted studies on the relationship between pulmonary cancer and silicosis by gathering clinical data of 2,815 miners working at the Sado Mine (Mitsubishi Mining Co., Ltd.). Figures indicate that tubercular complications increase with the progress of silicosis, especially with patients over 40 years of age. The

exposure period of the silicotic cases examined was sufficiently long enough to develop pulmonary cancer, if the facts of KLOZT and others are true, but none was detectable by X-ray examination. The development of silicosis depended not only upon the amount of silica dust inhaled but also upon the duration of the exposure and the individual constitution. Thus, the inhalation of silica dust particles does not necessarily lead to pulmonary cancer. The statistical figures are published in the J. Niigata Med. Assn. (Japan), 60, No. 3, 1-4 (1946).

(2) Doctors Ken SAITO, Ichiro SATO, and Kaneyoshi AKAZAKI studied the clinical reports and conducted post mortem examination of 6 human cases of silicosis to determine its causes. The results were published in the J. Hokuetsu Med. Assn. (Japan), 59, No. 6, 655-674 (1944). At the present time Dr. Ken SAITO is the Head of the Osarizawa Mine Hospital and Dr. Ichiro SATO is Head of the Sado Mine Hospital, both hospitals belonging to Mitsubishi Mining Co., Ltd. A brief summary by Dr. AKAZAKI in partial fulfillment of the request is as follows:

(a) The relationship between the chemical composition of the dust particles inhaled and the changes in the tissures are as follows:

The chemical composition of the mine dust particles was analyzed by Dr. Ken SAITO (J. Hokuetsu Med. Assn. (Japan), 59, No. 6, 675-698 (1944)) to be 87.25% SiO_2, of which 90% was free silica and 10% silicates; 3.98% Fe_2O_3; 4.33% Al_2O_3; 0.11% MnO_2; 0.74% CaO; 0.35% MgO; and 1.40% S. It is concluded that the inhalation of free silica is the dominant factor in the genesis of silicosis. The amounts of Fe_2O_3, MnO_2, Al_2O_3, CaO, MgO, and S were in too small a percentage to give any appreciable effect upon the pulmonary changes.

Upon micrographical and histological examination, a fairly large amount of soot dust (presumably from the miner's lamp) was found deposited with silica dust in the tubercular foci. Such soot dust was found experimentally in rabbits to be harmless and causes no tubercle formation or fibrous proliferation in the lymphatic nodules of the lung and the pulmonary hilus according to K. AKAZAKI and Fujio NITTONO, (Trans. Soc. Path. (Japan) 31, 326-333 (1941), Inclosure 10). Thus, the presence of coal or soot dust is insignificant in the formation of tubercle or hardening of the lung tissues.

(b) The relationship between the pathological changes and the duration of exposure depends upon the amount of silica dust particles inhaled and the working conditions. The number of dust particles having diameters less than 5 μ afloat in 1 mm^3 were obtained under varying conditions with a Zeiss konimeter as follows: 810 for drillers, 240 for miners, 350 for timber men, and 360 for transporters. The progress of pathological chances in the lungs is proportional to the quantity of dust particles present in the atmosphere and to the actual exposure time. It has been known to medical researchers (ICKERT, GUTZEIT, GROETSCHEL, BERGERHOFF, etc.) that in all types of pneumoconiosis, particularly silicosis, the genesis and progress of the disease is also dependent upon the disease suspectibility of the individual. This view point was experimentally affirmed by Dr. Sumito TAKEUCHI (J. Hokuetsu Med. Assn. (Japan) 59, 306-327 (1944), Inclosure 11) as a result of his own animal experiment in that when sufficient silica dust is inhaled to cause silicosis, the disease automatically progresses even after no more silica dust particles are inhaled. Silicotic tubercles are commonly believed to appear evenly and symmetrically on both lungs, but this is true only when silicosis is not complicated by some other disease.

were radiologically and histologically established. A rather large number of coal miners had anthracosis, their pneumoconiosis lesions due to the presence of silica in the coal dust. Many patients had also tuberculosis in addition to the pneumoconiosis producing fibrous proliferation in the lymphatic systems of the lung and the pulmonary blood capillaries (V. ... and ... ... (... 22, ...-... (1941)). Reference ...: the inhalation of coal or soot dust is responsible for the formation of ... in ... of the ... lungs.

... ... the duration of exposure ... the number of silica dust particles inhaled and the working conditions. The number of dust particles ... diameter less than 5 μ inhaled ... the ... as follows: ... for ... ... ; 150 for timber men, and ... for ... ... The progress of pathological ... in the lungs is proportional to the ... of dust particles present in the atmosphere and to the actual exposure time. It has been ... by medical ... (... ... ...) that in all these ... pneumoconiosis, particularly silicosis, the ... and progress of the disease ... upon the disease susceptibility of the ... ... view point ... ... (... 12, ...-... (1941)), ... in ... ... silica ... the disease ... progress ... after no more silica dust particles are ... are ... ... is ... when ... in ... of ... .

(c) Silicosis is more likely to commence in the deeper recesses of the lungs remote from the pleura than in the pulmonary hilus or the sub-pleura except when the lymphatic nodules undergoes pathological changes. This is confirmed by X-ray examinations conducted by Dr. Ken SAITO (J. Hokuetsu Med. Assn. (Japan), 59, No. 6, 675-698 (1944)), but conflicts with the results of the animal experiment (AKAZAKI, NITTONO, TAKEUCHI, TAKAHASHI) in which the foci appeared more frequently near the sub-pleura.

(d) The histological findings are as follows:

Human silicotic tubercles are never formed by the organization of dust cells collected in the pulmonary alveolar cavities according to investigation conducted by Doctors Kaneyoshi AKAZAKI, Fujio NITTONO, and Sumito TAKEUCHI. They came into existence only after the silica dust particles filtered through the pulmonary alveolar walls, penetrated into the interstitial substances, and deposited. Post mortem examinations and past researches indicate that the metastasis of the dust particles takes place when they are transmitted in the free state by the lymph flow, but not by the pulmonary dust cells that have ingested the dust particles. This is conceivable from the fact that the pulmonary alveolar walls have an extremely thin structure and whatever dust particles found in the pulmonary lymph nodules and in the silicotic nodules of the other organs are all extremely small in size. Thus, only fine dust particles, less than 1μ in diameter, can filter into the interstitial substances and be injurious.

Silicotic tubercular are often found encircling or lying near the walls of the pulmonary blood vessels, suggesting some relationship between the appearance of the tubercles and the thickly located lymphatic vessels. Other tubercles are formed in the lympho-follicles lying around the bronchi, but comparatively rare in the pulmonary alveolar walls not in direct contact with the connective tissues or the blood vessels of the sub-pleura. The formation of these tubercles commences with the proliferation of the histiocytes

or fibrous granular cells that have ingested the silica dust and other dust particles. While the proliferation of such cells is in progress, the fibrous formation is not so pronounced, but with the growth and aging of the tubercles, the formation of lattice fibers became active, gradually gelatinized, and finally converted into hyaline tubercles. When the tubercles become hyloid, the silica or soot dust ingested by the cell begin to segregate and pass into the interstices of the collagenous fibers and settle. As the pathological process continues, the older tubercles become necrotic and amorphous in structure, then it is softened and resorbed leaving a hollow cavity which is not the result of tubercule bacilli. Dr. Kaneyoshi AKAZAKI, partially agreeing with SCHEID, believes that the immediate cause of the intra-tubercle formation of the hollow cavities or liquefaction of the connective tissues lies undoubtedly in the deterioration of the arteries supplying nutrition.

Giese's Theory that the silicotic tubercles first appear in the lympho-sinus or in the derivative nodulus of the cortical substances has been experimentally disapproved by Dr. K. AKAZAKI. The silicotic tubercles of the human lymph nodules do not commence in the lympho-sinus but mainly in the parenchyma. It was further experimentally proved that the tubercles originate, aside from the small derivative nodular sections, more in the peripheral portion of the cortical substances.

With regards to the metatasis of silica dust particles into the peritoneal cavities, the utter absence of any silicotic process in the lymph nodules of the mesenteriums led Dr. Kaneyoshi AKAZAKI and students to conclude that no dust particles are absorbed by the mesentery walls or transported by the blood circulation (haemotogeneous metatasis) as the appearance of the pathological process is always too localized and not diffusive enough to justify the assumption of haemotogeneous matatasis. The last plausible alternative appears to be the retrogressive lymphatic metatasis.

[illegible] particles, [illegible] position. [illegible] proliferation of such cells is in progress, [illegible] formation is not so pronounced, but with the growth and [illegible] of the tubercles, the [illegible] of lattice fibers become active, gradually gelatinized, and finally converted into [illegible] tubercles. When the tubercles become [illegible] silica or soot mass ingested by the cells [illegible] aggregate and pass into the interstices of the collagenous fibers and settle. As the [illegible] [illegible] continues, the older tubercles [illegible] [illegible] [illegible] which is not the result of tubercle bacilli. [illegible], partially agreeing with [illegible], believes that the immediate cause of the [illegible] formation of the hollow cavities [illegible] of the connective tissues [illegible] in the determination of the [illegible] [illegible].

[illegible] theory that the silicotic tubercles [illegible] in the lymph-stream or in the [illegible] of the corneal substances [illegible] [illegible] discovered by Dr. [illegible]. The [illegible] of the human lymph [illegible] not recovered in the lymph-sinus [illegible] the mesenteries. It was further [illegible] that the tubercles [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] of the [illegible] [illegible].

[illegible] regards to the metastasis of silica [illegible] particles into the peritoneal cavities, [illegible] [illegible] of my silicotic process in the lymph [illegible] the mesenteries led Dr. [illegible] [illegible] students to conclude that [illegible] [illegible] [illegible] transported by the blood currents [illegible] [illegible] appearance of the pathological process is always too local [illegible] diffusive enough to justify the assumption of haematogenous metastasis. The last [illegible] [illegible] appears to be the retro[illegible] [illegible] [illegible].

Tubercular formation are induced by haematogeneous metatasis since tubercle foci were found to appear in the various organs, especially in the liver, spleen, and bone medulla rich in reticular endothelial cells. This was proved by Dr. Sumito TAKEUCHI (J. Hokuetsu Med. Assn. (Japan), 59, 306-327 (1944), Inclosure 11), in his laboratory experiment by injecting silica dust emulsion into the vein of rabbits.

(e) The relationship between silicosis and tuberculosis was studied from two angles; first, the effect of the tuberculosis complication upon the pre-existing silicotic foci, and second, the effect of silica dust particles upon the pre-existing tuberculosis. No definite explanations have been found, but Dr. K. AKAZAKI believes that the proliferation process based upon results of histological examinations, does not necessarily take place and the exudative tubercular foci often appear concurrently with silicosis.

The microscopic examination of the effect of silica dust particles upon tuberculosis revealed the presence of some adhesive foci, resembling the so-called "adhesive silicotic tubercles", but in contra-distinction to the normal adhesive silicotic tubercles, their centers were ashy in color, suggesting the progress of caseation of tuberculosis. This was ascertained as caseation of tuberculosis by carefully examining those tubercular foci that had embodied only coal dust in their peripheral films. These foci were encircled by a sort of proliferated granular tissues which embodied larger numbers of initial silicotic tubercles than were found elsewhere in the lung field causing the neighboring lung region to be hardened. In other words, the dust stimulated the proliferation of the granular tissues to such an extent that they injured the function of the neighboring lung field, whereas the silica dust checked the caseation process in the center of the foci. The extremely aggressive granular formation was brought about by the inhalation of the silica dust due to the rapid response of the inflammatory

[illegible] experiment by injecting silica dust [illegible] the vein of rabbits.

(e) The relationship between silicosis and tuberculosis was studied from two angles; first, the effect of the tuberculosis complication upon the pre-existing silicotic foci, and second, the effect of silica dust particles upon the pre-existing tuberculosis. No definite conclusions have been found, but Dr. K. [illegible] believes that the proliferation process based upon results of histological examination, does not necessarily take place and the exudative tubercular foci often appear concurrently with silicosis.

The microscopic examination of the effect of silica dust particles upon tuberculosis revealed the presence of some exudative foci, resembling [illegible] of tuberculosis by carefully examining tubercular foci that had embedded only [illegible] in their peripheral films. These foci were encircled by a sort of proliferated granular tissues which enclosed a larger number of [illegible] tubercles than were found elsewhere in the [illegible] field causing the neighboring lung tissue to be hardened. In other words, [illegible] proliferation of the granular tissues to such an extent that they [illegible] the neighboring lung tissue, while the silica dust checked the [illegible] process in the center of the foci. The extremely extensive granular formation was brought about by the inhalation of the silica dust due to the rapid response of the [illegible]

tubercular process to the complication. Thus, the inhalation of silica dust particles stimulates the growth of the abnormally aggressive granular tissues around the tubercle foci and makes the prognosis of tuberculosis worse instead of exerting curative effects.

(3) Dr. Sumito TAKEUCHI conducted research on the pathogenesis of silicosis under the direction of Dr. Kaneyoshi AKAZAKI during 1943-1944 at the Niigata Medical College. Rabbits were subjected to experimentation and the results were published in the J. Hokuetsu Med. Assn. (Japan), 59, 306-327 (1944), Inclosure 11. The results obtained were as follows: (a) The finer silica dust particles are more conducive to the development of silicosis due to the ease of filtering through the alveolar walls and conveyed to other parts of the body by haemotogeneous metatasis, and (b) the dust particles penetrating into the body of the rabbit, either by forced inhalation or by injection, was conjested by the cells of the reticular endothelial series giving rise to the proliferation of the lattice form fibers which are collagenized and finally resulted into typical silicotic tubercles.

(4) Doctors Kaneyoshi AKAZAKI and Fujio NITTONO (Trans. Soc. Path. Japan, 31, 326-333 (1941), Inclosure 10) have classified the morphological changes of the respiratory tract caused by various types of inhaled dust particles by post mortem examination of human bodies and by experimental researches on pneumoconiosis with different animals. They have discovered the remarkable appearance of the alveolar groups fully packed with carbon soot dust accompanied by distinctly thickened walls and pronounced state of atrophy. This phenomena appeared to be a protective process of the lungs against the intrusion of the soot dust which is embodied in the atrophied alveoli. However, it is highly probable but not conclusive that a certain amount of fine soot particles penetrated into the lung interstices in a free state by way of the lymphatic circulation. The metastatic deposition of soot dust in the lymphatic nodules of the pulmonary hilus was observed to commence first with a sporadic migration in the cortical nodules and the medullary cord mostly ingested by the reticular cells or settled in a free state in the tissue crevices.

However, in the course of time the soot dusts gradually tended to assemble in masses on the inner brim of the cortical nodules or in the medullary cords. The proliferation of the lattice and connective tissues fibers were not observed and it may be concluded that the presence of soot dust causes no fibrous reactions.

(5) Dr. Fujio NITTONO conducted systematic macroscopical and histological examination of 108 cases of autopsy of human lungs affected by inhalation of coal dust particles. The findings are reported in his paper entitled "Contribution to the Study of Human Pulmonary Anthracosis," published in the Trans. Soc. Path. Japan, 30, 290-296 (1940), Inclosure 12. The quantity and the type of coal dust deposition in the 108 cases of autopsy of human lungs and the adjacent organs are abstracted and tabulated from the original report entitled "Studies on the Deposition of Coal Dust in the Human Lungs and its Migration," published in the Hokuetsu Med. J. (Japan), 55, No. 4, 210-291 (1940), Inclosure 13.

(6) Dr. Setsugi SAKAI has conducted an animal experiment during the latter part of World War II to determine the influence of silicotic processes upon the pulmonary tuberculosis. The results of the experiment are published in the J. Niigata Med. Assn. (Japan), 62, 1-10 (1948), Inclosure 14.

(7) Dr. Koji TAKAHASHI conducted an animal experiment with rabbits for 107 weeks duration to examine how the injected iron dust will affect the lungs and other organs. Also, the inhalation of ferric oxide dust was conducted for a maximum period of 914 days to study how the minute particles passed from the alveolar cavities into the interstitial substances. The results of this experiment coincided with that of Professor AKAZAKI's on experimental anthracosis (Trans. Soc. Path. Japan, 31, 326-333 (1941). Free iron dust particles were often found settled in the inter-tissue substances of the alveolar walls, bronchi, and blood vessels, as well as in the inter-lymphatic spaces and vessels. Only a very small portion of the iron oxide particles, if any, was ingested by the histocytes or the connective tissue cells. When compared with anthracosis, the iron oxide dust inhalation or injection brought about only a small dust

deposition even when the experiment was conducted over a long period but no proliferation of the lattice or connective tissue fibers were detected. The details and the results of the experiment are published in the Res. Rept. Path. Dept., Niigata Med. College (Japan), 60, 1-21 (1944), Inclosure 15.

f. Dr. Ugaro KOINUMA of the Department of Hygiene, Nagoya University, recalled the research work of Dr. Masao YAJIMA, who conducted pathological studies on the experimental pneumoconiosis in guinea pigs and its relationship with tuberculosis during 1932 and 1933 at this laboratory. The results of the experiment are published in the Memoirs of Path. (Japan), 10, No. 1, 1-135 (1935), Inclosure 16. The last experiment conducted on pneumoconiosis at this laboratory was that of Dr. Hiramasa SENDA on the "Research of Cementosis," which was published in the National Hygiene (Japan), Vol (?), 672-695 (1944), Inclosure 17.

Reference was secured to the research work conducted by Dr. Kiyoyoshi HORIGUCHI during 1933 and 1934 at the Department of Hygiene, Osaka University, on the inhalation of microscopic foreign particles. The results of the experiment are published in the J. Osaka Med. Assn. (Japan), 35, 365- (1936); ibid, 35, 547-551 (1936); and ibid, 35, 663-668 (1936), Inclosure 18. In this project, Dr. Kiyoyoshi HORIGUCHI studied the inhalation of microscopic foreign substances by healthy animals, by animals with lungs atrophied prior to inhalation, and by animals with lungs atrophied after the commencement of dust inhalation to determine in which pulmonary region the greatest amount of dust particles (soot dust, carmine pigment, and zinc oxide dust) would settle. In the experiment with normal animals, rabbits, dogs, and goats, the inhaled foreign particles settled in greater amounts in the right upper lobe of the lungs. When the lungs of goats and rabbits were atrophied by pneumothorax, phrenicectomy, and thracoplasty methods, the pulmonary regions contained the least amount of dust deposit due to the highly impeded respiratory function; whereas the region only slightly affected had a comparatively large deposits.

g. Dr. Tsuneo HASEGAWA of the Mitsubishi Mining Co., Ltd., Research Laboratory; Saitama-ken, Omiya-shi, Kitabukuro, 16, is actively conducting experimental research on the migration of fine silica dust particles, less than 5 μ in diameter, in the body of rabbits. The objective of the experiment is to determine the extent of silica dust particle deposition in the spleen, heart, liver, and lymphatic systems by subcutaneous injection of sericite solution into the veins of the rabbits. The experiment was commenced in May 1947 by hand grinding the sericite (approximately [illegible]0% SiO_2) obtained from Ibaraki-ken, Hitachi-shi area to less than 5 μ diameters. A 2% emulsion was prepared and 2 cc/kg weight of the rabbit is subcutaneously injected at regular intervals. At the present

condition even when the experiment was conducted with a long period but no proliferation of the nodules or concentric silicotic fibers were detected. The details and the results of the experiment are published in the Jour. Nat. Tech. Sch., Hiroshima Med. College (Japan), [illegible] (1944), Enclosure 15.

3. Dr. Kyoto KOJIMA of the Department of Hygiene, Nagoya University, continued the research work of Dr. Masao YAMADA, who conducted pathological studies on the experimental pneumoconiosis in guinea pigs and its relationship with tuberculosis during 1936 and 1939 at this laboratory. The results of the experiment are published in the Nagoya J. of Path. (Japan), 13, No. 1, 1-135 (1943), Enclosure 16. The last experiment conducted on pneumoconiosis at this laboratory was that of Dr. [illegible] [illegible] on the "Research of Pneumoconiosis," which was published in the [illegible] [illegible] (Japan), Vol [illegible], [illegible]-625 (1944), Enclosure 17.

Reference was secured to the research work conducted by Dr. [illegible] KOBAYASHI during 1933 and 1934 at the Department of Hygiene, Osaka University, on the inhalation of experimental foreign particles. The results of the experiment are published in the J. Osaka Med. Assn. (Japan), 33, 385- (1934); ibid, 33, 549-581 (1934) and ibid, 33, [illegible] (1934), Enclosure 18. In this project, Dr. KOBAYASHI [illegible] studied the inhalation of [illegible] foreign particles in various animals, by animals with large [illegible] [illegible] prior to inhalation, and by animals with large atrophied after the commencement of dust inhalation to determine in which pulmonary region the greatest amount of dust particles (soot dust, carmine pigment, and zinc oxide dust) would settle. In the experiment with normal animals, rabbits, dogs, and goats, the inhaled foreign particles settled in greater amounts in the right upper lobe of the lungs. When the lungs of goats and rabbits were [illegible] [illegible] [illegible], [illegible] [illegible] [illegible] [illegible] regions, the pulmonary regions contained the least amount of dust deposit due to the [illegible] lowered respiratory function, whereas the region only slightly affected had a comparatively large deposits.

4. Dr. Tsuneo HASEGAWA of the Mitsubishi Mining Co., Ltd., [illegible] [illegible], [illegible], [illegible], [illegible] II, is actively conducting experimental research on the migration of fine silica dust particles, less than 5 μ in diameter, in the body of rabbits. The objective of the experiment is to determine the extent of silica dust particle deposition in the spleen, heart, liver, and lymphatic systems by [illegible] injection of sericite solution into the veins of the rabbits. The [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] obtained from Ibaraki-ken, Hitachi-shi area [illegible] [illegible] [illegible] [illegible]. A 2% solution was prepared and 2 cc of [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] at regular intervals. At the present

time 15 animals are being treated. A rabbit is killed at regular intervals to make a macroscopical and histological observations of the changes in the different organs. This experiment is expected to be carried out another 6 months in order to obtain results over an extended period of time.

When the necessary preparations are completed, a series of dust inhalation experiments with rabbits will be commenced to correlate the results presently obtained as well as to determine the particle size distribution and the mode by which the silica dust particles penetrate to the various organs from the respiratory tract.

At the present time plans are being made with the electron microscope manufacturers to have photographs made of the silica dust particles settled in the different organs for possible determination of the dust particle sizes. If the electron microscope produces satisfactory results, the Mitsubishi Mining Co., Ltd., is seriously contemplating purchase of the instrument to carry out studies on the size distribution of dust particles in the various sections of the respiratory tract and other organs.

Dr. T. HASEGAWA was graduated from the Niigata Medical College in 1936 and conducted post-graduate studies on the problems of silicosis under Dr. Kaneyoshi AKAZAKI for one year. After joining the Mitsubishi Mining Co., Ltd., as a member of the medical staff, Dr. HASEGAWA has continued his studies on silicosis and has maintained a close relationship with Dr. AKAZAKI.

With regards to research projects conducted on dust particles at other Mitsubishi Mining Co., Ltd., plants, Dr. HASEGAWA disclosed the following information:

(1) Doctors Goro ITO and Mishio HAYAKAWA of the Teine Mine; Hokkaido, Sapporo-gun, Teine-mura, are conducting studies with Professor Zenjuro INOUYE on the effect of inhaling aluminum powder (imported from United States through Takeda Pure Chemical Co., Osaka, prior to World War II) to determine whether or not fibrous can be formed in rabbits. Preliminary results thus far obtained indicate that the pulmonary fibrous will not form in 6 months when aluminum powder is inhaled together with the silica dust particles. Professor Z. INOUYE is with the Department of Hygiene, Faculty of Medicine, Hokkaido University and he conceived of the idea approximately 10 years ago of utilizing fine aluminum powder through inhalation as a preventative measure against silicosis, but failed to commence the experimentation until 1946. Professor INOUYE's research work is along the similar line conducted by Dr. R.D. IRVIN at the Mining Laboratory of MacIntyre Porcupine Mine Ltd.

[illegible] This experiment is expected [illegible] 6 months in order to obtain results over an extended period of time.

When the necessary preparations are completed, a series of dust inhaling experiments with rabbits will be conducted to correlate the results obtained as well as to determine the particle size distribution and [illegible] of the silica dust particles in the animals [illegible].

At the present time plans are being made with the electron microscope [illegible] to have photographs made of the silica dust particles settled in the different organs for possible determination of the size [illegible]. If the electron microscope produces satisfactory results, the Mitsubishi Mining Co., Ltd., is seriously contemplating purchase of the instrument to carry out studies on the size distribution of dust particles in the various sections of the respiratory tract and other organs.

Dr. T. [illegible] was graduated from the Niigata Medical College in [illegible] and conducted post-graduate studies on the problems of silicosis under Dr. [illegible] AKAZAKI for one year. After joining the Mitsubishi Mining Co., Ltd., as a member of the medical staff, Dr. [illegible] has continued his studies on silicosis and has maintained a close relationship with Dr. [illegible].

With regards to research projects on [illegible] dust particles at other [illegible] Mining Co., Ltd., [illegible], Dr. [illegible] furnished the following information:

(1) [illegible] Presently, [illegible] on the [illegible] prior to World War II [illegible] be formed [illegible]. From many results [illegible] particles. Professor [illegible] to take the [illegible] Faculty of Medicine, [illegible] University and [illegible] years ago [illegible] but failed to [illegible] until 1946. [illegible] research work [illegible] at the [illegible] Mining Laboratory [illegible].

Pathological and histological studies are also conducted by Doctors ITO and HAYAKAWA on the mechanism by which the silica dust particles are enveloped by the aluminum metals. The presence of aluminum metal about the silica dust particles embedded in the different parts of the respiratory tract is detected by the use of aurine indicator. The relationship between tubercule baccilli, silica dust particles, and aluminum powder is being conducted. The final results of the animal experiment will not be completed until 1949.

(2) Dr. Ken SAITO, Head of the Osarugawa Mine Hospital, Akita-ken, Kazuno-gun, Kazuno-mura, Osarugawa-machi, and Dr. Ichiro SATO, Head of the Sado Mine Hospital, Niigata-ken, Sado-gun, Aikawa-machi, are presently not conducting any experimental researches on silicosis. Doctors K. SAITO and I. SATO are both graduates of the Niigata Medical College and both have conducted research work under Professor Kaneyoshi AKAZAKI with whom they maintain close relationship concerning problems in silicosis.

6. CONCLUSIONS: Ten Japanese medical authorities were interviewed in the course of the investigation. A number of these have conducted a series of animal experiments and post mortem autopsy of human beings afflicted with pneumoconiosis. However, no experiments have been conducted to any great detail on the size distribution of the microscopical particles lodged or deposited in the different anatomical parts of the respiratory tract. The results obtained from Japanese research projects, both published and unpublished, with respect to the point of deposition, size of the particles, and the pathological changes are tabulated in Table I.

TABLE I.

Researcher	Reference to Inclosures	Deposition of Particles	Distribution of Inhaled Particle size	Pathological Changes
S. ISHINISHI and S. TAKEYA	1	No deposition of limestone particles (4.24% SiO_2 and high carbonate content) found in lung	61.6% >180 mesh	Noted congestion, dropsy, hemorrhage, and alelectase in lungs; epithelium ablution in trachea; and epithelium necrosis in larynx
T. MIYAZAKI and G. NIWA	2	Deposition occurred in lymphatic glands of pulmonary hilus with Cottrell dust (39.93% SiO_2)	50.7% >300 mesh	Sub-acute laryngitis and trachitis

Pathological and histological studies are also conducted by Doctors [illegible] and [illegible] on the [illegible] by which the silica dust particles are [illegible] by the [illegible]. The [illegible] of aluminum metal about the silica dust particles [illegible] in the different parts of the respiratory tract is [illegible] by [illegible]. The relationship between tubercle bacilli, silica dust particles, and aluminum powder is being continued. The final results of the animal experiments will not be completed until 1949.

(2) Dr. Ken SAITO, Head of the [illegible] Mine Hospital, Aikawa-machi, [illegible], and Dr. I. SAITO, Head of the Sado Mine Hospital, Niigata-ken, Sado-gun, Aikawa-machi, are [illegible] experimental research on silicosis. Doctors K. SAITO and I. SAITO are both graduates of the Niigata Medical College and both have conducted research [illegible] close relationship concerning problems in silicosis.

3. [illegible]. [illegible] in the course of the investigation. A number of these have conducted a series of [illegible] infected with pneumoconiosis. However, no experiments have been conducted in as great detail as [illegible] located or deposited in the different anatomical parts of the respiratory tract. The results [illegible], published and unpublished, with respect to the point of deposition, size of the particles, and the pathological changes are tabulated in Table I.

TABLE I.

Researcher	Reference to Sources	Deposition of Particles	Description of Inhaled Particle size	Pathological Changes
1. [illegible] and 2. [illegible]	1	[illegible] limestone particles ([illegible] SiO_2) and high carbonate content) found in lung	[illegible] mesh	[illegible] and [illegible] in lungs, epithelium ablation in bronchi, and epithelium necrosis in larynx
3. [illegible] and 4. [illegible]	2	Deposition occurred in lymphatic glands of pulmonary [illegible] ([illegible] SiO_2)	[illegible] mesh	[illegible] laryngitis and tracheitis

H. ODA	3	Cotton, wool, and staple fibers deposited in alveoli	33-40% less than 100 μ in length	Deposition caused vicarious emphysema but no proliferation of connective tissues
I. KURODA	4	Silica dust (89-93% SiO_2) deposited in alveoli	90% less than 5 μ in dia.	Pulmonary alveolar septa was partially infiltrated with diffusive round cells and proliferated; etc.
K. TAKEUCHI and M. YANAGIBASHI	9	Inhalation of SO_2, H_2S, and CS_2	Fine mist	Formation of vesicles due to degeneration and collapse of epithelial cells of trachea
K. KOBAYASHI	---	Deposition of silica dust (47-57% free silica) in alveoli	72.6% less than 1 μ in diameter	Disintegration of pulmonary alveoli, proliferation of bronchial epithelial cells, etc.
K. SAITO I. SATO and K. AKAZAKI	---	Deposition of silica dust (87.25% SiO_2) in the tubercular foci of human lung	50-60% less than 5 μ dia.	Penetration of silica dust particles through pulmonary alveolar walls into interstitial substance where deposition take place. Only particles less than 1 μ in dia. can filter through tissue
K. AKAZAKI and F. NITTONO	10	Deposition of soot dust in alveolar cavities	Inhalation of carbon soot	Soot dust particles not received by bronchial epithelium or resorbed through intercellular lymphatic crevices; passage of soot dust from alveolar cavities into interstices was not definite
S. TAKEUCHI	11	Silica dust particles (95% SiO_2) in alveolar cavities	50-60% less than 5 μ dia.	Formation of silicotic tubercules by collagenization of proliferated lattice-form fibers due to the congestion of reticular endothelial cells

F. NITTONO	12	Coal dust deposited in human lungs, namely, alveoli	Mine dust	Coal dust particles on the peripheries of alveolar walls, transported through lymphatic vessels to glands, or ingested by interstitial connective tissues. Especially dense deposition in peri-bronchial, perivascular, and sub-pleura connective tissues
S. SAKAI	14	Injection of silica emulsion and tubercle bacilli	—	Alveolar walls were thickened by deposition of silica dust. Symphatic nodules showed only diffusively proliferated epithelial cellular tubercles
K. TAKAHASHI	15	Ferric oxide dust particles was deposited in intertissue substances of alveolar walls, bronchi, and blood vessels	Commercial ferric oxide powder	Proliferation of epithelial cells of alveolar walls and occlusion of free ferric oxide dust particles. However, no permanent change of the alveolar walls occurred.
M. YAJIMA	16	Dust particles (83% SiO_2) deposited in bronchial and alveolar cavities	Fine dust on streets of Nagoya	Surface of lungs showed deposition of dust particles as black spots; right pulmonary appex was most affected. Complications arose when injections of tubercle bacilli were given.
H. SENDA	17	Cement dust (22.2% SiO_2) deposited in alveoli and other points	67% less than 5 μ dia. of which 10.5% less than 1 μ dia.	Many dust particles gathered around blood vessels, lymphatic vessels, and bronchus where engorgement by dust cells were taking place; dust particles were isolated in pulmonary vesicle walls, cell walls, and cell spaces

K. HORIGUCHI	18	Right upper lung in larger quantity than other portions	Soot dust, carmine pigment, and zinc oxide separately	Comparison of the amount of dust particles deposited in each region of lungs was made
T. HASEGAWA		Sericite emulsion (50% SiO_2) injected into animals	Dust ground to less than 5 μ dia.	Experiments are under way at the present to determine mechanism by which dust particles migrate from alveoli to other organs

At the present time Dr. Tsuneo HASEGAWA, Research Laboratory of the Mitsubishi Mining Co., Ltd., Saitama-ken, Omiya-shi, Kitabukuro, 16, and Doctors Goro ITO and Mishio HAYAKAWA, Teine Mine of Mitsubishi Mining Co., Ltd., Hokkaido, Sapporo-gun, Teine-mura, together with Professor Zenjuro INOUYE, Department of Hygiene, Faculty of Medicine, Hokkaido University, are actively conducting animal experiments on the study of pneumoconiosis. Professor Kaneyoshi AKAZAKI is acting as consulting pathologist and conducting pathological studies on the specimens submitted by the medical researchers of Mitsubishi Mining Co., Ltd. Conclusive results of their present research projects will not be known until Spring 1949.

7. RECOMMENDATIONS: Recommend that this report be forwarded to Targets Branch, Department of the Army (Strategic) Intelligence Division, for collation.

Frederick G. Bull

FREDERICK G BULL
Major, FA
Commanding

18 Incls:

1. "Injurious Effects of Rock Powder used in Coal Mines upon the Respiratory Organs, (1) Experiment with "SS" Rock"
2. "The Influence of the Rock Powder used in the Coal Mines upon the Human Body"
3. "Experimental Studies on the Influences of Textile Fibers on the Lungs of Rabbits and the Development of Tuberculosis"
4. "Experimental Study on the Correlation between Silicosis and Pulmonary Tuberculosis"

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]		[illegible]	Dust ... 1948 ... 5, ...	[illegible]

At the present time ..., Tsuneo [illegible], Research [illegible] ... Mining Co., ... [illegible] ... and ... [illegible] ... HAYASHI, ... [illegible] ... University, are ... conducting animal experiments on the study of [illegible]. Professor ... [illegible] is acting as ... [illegible] ... Mining Co., Ltd. ... results of their present research projects will not be known until [illegible].

7. RECOMMENDATIONS: Recommend that this report be furnished to [illegible]

[illegible]

(1) Incls:

1. "Injurious Effects of Rock Powder used in Coal Mines upon the Respiratory Organs, (1) Experiment with "S" ..."
2. "The Influence of ... Rock Powder ... [illegible] ... the ... Body"
3. "[illegible] ... and the Development of Tuberculosis"
4. "Experimental Study on the Correlation between [illegible] and [illegible]"

5. "Discharging Process and the Expelling Velocity of Inhaled Dust in the Trachea"
6. "Comparative Study of Dust Expelling Velocity of Trachea of Various Species of Animals"
7. "Influence of Various Physico-chemical Conditions upon Dust Expelling Function of Trachea"
8. "Comparative Study of Dust Expelling Velocity in Trachea of Animals of Various Ages"
9. "Pathological Changes of the Mucous Membrane of Trachea by Continuous Inhalation of Various Poisonous Gases and Their Relationship with Foreign Body Expulsion Action"
10. "Experimental Contribution to the Study of Pulmonary Anthracosis in Rabbits"
11. "Experimental Research on the Pathogenesis of Silicosis"
12. "Contribution to the Study of Human Pulmonary Anthracosis"
13. "Studies on the Deposition of Coal Dust in the Human Lungs and its Migration"
14. "Research on the Influences of Silicotic Processes upon the Pulmonary Tuberculosis"
15. "Experimental Research in Pulmonary Siderosis"
16. "Study on the Pathological and Anatomical Process of Pneumoconiosis Artificially Caused in Guinea Pigs and Their Relationship with Pulmonary Tuberculosis"
17. "Research on Cementosis, Part II Experimental Studies pertaining to Cementosis"
18. "Research Concerning Inhalation of Microscopic Foreign Substances, Parts I, II, and III"

INJURIOUS EFFECT OF ROCK POWDER USED IN COAL MINES UPON THE RESPIRATORY ORGANS (1) EXPERIMENT WITH "SS" ROCK (White Rock Powder)

by

Shiko TAKEYA and Susumu ISHINISHI
Pathological Research Laboratory, Mitsui Medical Institute for Industry of Mitsui Mining Co., Ltd., Fukuoka-ken

ABSTRACT

(Full Report Unpublished; Abstract published in Igaku to Seibutsugaku, 11, No. 4, 235-239 (1947))

As an effective method of counteracting coal dust explosions, the Japanese Government Coal Mine Explosion Control Regulations require the sprinkling of rock powder in every mine (a) to prevent coal dust from floating in the atmosphere, (b) to minimize the inflammability of coal dust by increasing the content of incombustible substances in the coal dust, and (c) to minimize damages to within a limited section in the event of explosion.

The objective of the present research is to examine the influences of the various types of rock powder upon the respiratory organs and to determine the suitability of rock powder from the medical standpoint.

1. Experimental Method:

a. Test Animals: Matured rabbits
b. Rock Powder: Limestone pulverized into fine powder by a crusher:

(1) Chemical composition was as follows:

Chemical Component	CO_2	SiO_2	Al_2O_3	Fe_2O_3	MnO	CaO	MgO	SO_3	Na_2O
Distribution %	40.850	4.240	1.729	1.071	0.279	51.000	0.869	0.583	0.074

NOTE: pH 7.90 (Obtained by dissolving 1 g. of rock powder in 100 cc. of distilled water, pH 5.5)

(2) Size of the rock powder grains was as follows:

Grain Size, Mesh	180	180-76	76-30	30-20	20
Distribution %	61.6	18.6	14.0	4.4	1.4

(3) Shape of rock powder: The rock powder was mixed in water to make a suspension in solution and one drop of the solution was examined under the microscope. The grain of the rock powder was found to have round or nearly round polygon shape.

c. Dust Inhalation Method: A wooden box (190 x 94 x 120 cm) was partitioned into 48 small cages, each measuring approximately 28.8 x 42.5 x 28 cm. One rabbit was placed into each cage and then the rock powder was admitted continuosly into the box by means of a blower from the upper part of the inhalation box, Figure 1.

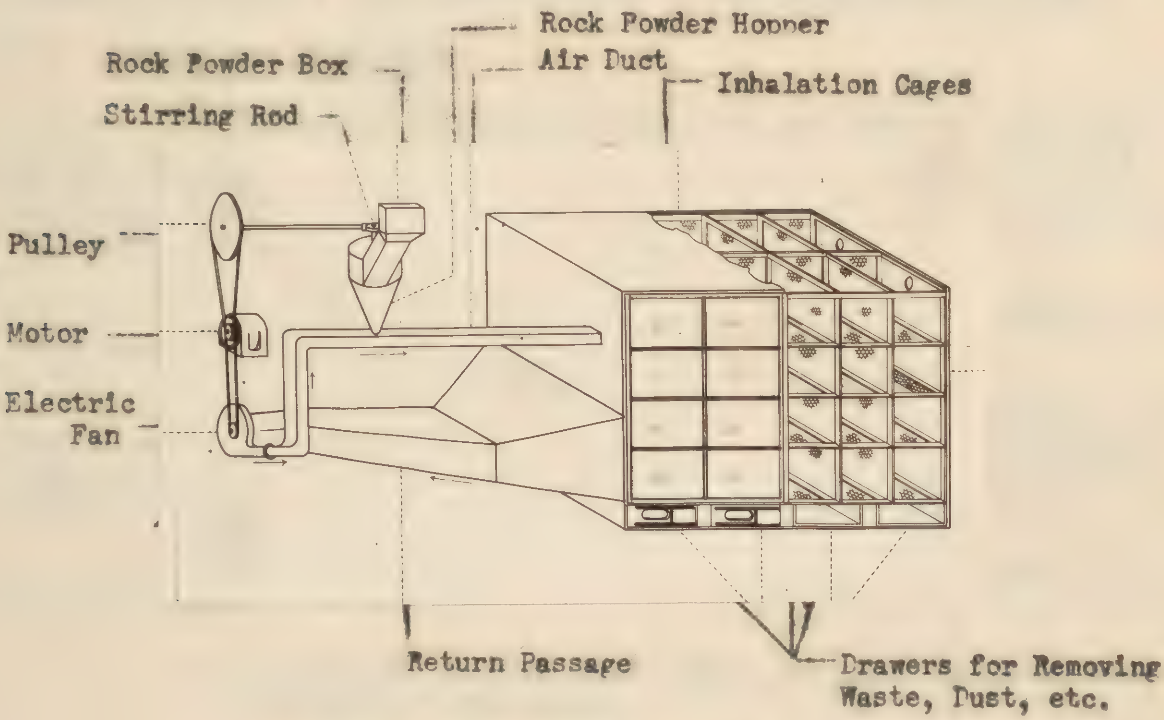


FIG. 1 INHALATION APPARATUS

d. Duration of Rock Powder Inhalation: The experiment was commenced from 10 Jun 40. A rabbit was placed in each cage about 0900 hours after their morning feeding every day except holidays. The inhalation of dust was continued until 1600 - 1700 hours and taken out of the cage. During the summer months, the experiment was suspended about 1300 hours. The inhalation time was approximately 5 to 8 hours/day and the treatment was continued until all the animals died.

e. Method of Examination: After the dead animals were dissected, each viscera was extracted and fixed with 10% formalin, washed with water, and finally dehydrated with alcohol. Then colloidin slices were made of the specimen in the conventional manner. For staining the specimen haematoxylin-eosine dye was usually used unless van Giesen and azine staining were required.

2. Experimental Results:

The results of the examinations are summarized in Tables 1 and 2. The notations, (+ + +), (+ +), (+), etc., are only arbitrarily selected by the authors to indicate the relative extent of the pathological changes.

3. Summary and Discussion:

a. The difficulty involved in this study was that the concentration of the rock powder in the air blown into the inhalation chamber could not be quantitatively denoted. The rock powder was blown into the chamber under assimilated conditions comparable to that in coal mines, except for the difference in the humidity.

b. The life period of the test animals were relatively short, being from only 1 to 25 days.

c. The rock powders did not deposit in the lungs. So-called "dust cells" were not formed. This was probably due to the calcium carbonate, main constituent of the rock powder, being readily soluble in water due to the presence of carbon dioxide in the air.

d. The pathological changes in the respiratory organs were observed as follows:

(1) Congestion, dropsy, haemorrhage, bronchuli pnuemonia and atelectase in the lungs.

(2) Congestion, dropsy, and epithelium ablution in the trachea.

(3) Congestion, dropsy and epithelium necrosis in the larynx.

e. The repletion and loss of vitality of the lungs, necrosis of the larynx epithelium, pleurisy, etc., were also observed in a few cases.

TABLE I HISTOLOGICAL OBSERVATION OF THE LUNGS

Animal No.	Duration of Experiment days	Period of inhalation hrs.	[illegible]	Dropsy	Haemorrhage	[illegible]	Emphysema of the Lungs	Ablution Secretion of Bronchuli Epithelium	Pneumonia	Pleurisy	Remarks
54	1	2	+++	+++		+		+			Expansion of ventriculus dexter
80	1	11	++		+++	++	+	++			Haematoma-like substance, large as red bean, was found in apex of left lung. Inflammation phenomena of conjunctives.
84	2	[illegible]	+++	++	+	±		++			Slight haemorrhage under pleura
82	3	19	+++	+	+++	+		+	+++		Pneumonia nests were macroscopically observed
83	3	23	+++		++	++	+	++			
85	3	23	+++	+++	+		+	+++	+++		same as above
81	4	23	+++		+	++	+	++	+		
66	8	26				+++	+	++			Loss of vitality all over lungs
71	11	38.5	+++	+++				+			Slight haemorrhage was found in muscle layer of ventriculus sinister
79	13	52.5	+++	+	+		visible	+++	++		Inflammation phenomena of conjunctives in eye
75	14	54.5	[illegible]	[illegible]			+	+	+		
73	14	57.5	+++	++		±	+	+	+	+++	Surface of left lungs covered with ragged substance
51	22	79	+++	+++	+	+		+++	+++	++	same as above
72	23	84				+++		+++			Loss of vitality all over the lungs
63	24	88	++		+++	+++	+	+++			Haemorrhage observed in upper lobe of left lung

Incl 1, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE I HISTOLOGICAL OBSERVATION OF THE LUNGS (CONT'D)

61	24	89	+	++	+	+++	+	+++			
58	25	92	+++	+		-	--	+++	++	+	Moderately strong emphysema
65	25	96	++	++				+++			

NOTE: +, ++, and +++, are only arbitrarily selected by the author to indicate the relative extent of the pathological changes.

TABLE II HISTOLOGICAL OBSERVATION OF TRACHEA AND LARYNX

Animal No.	Duration of Experiment, days	Period of Inhalation, hrs.	Histological Observation of Trachea				Histological Observation of Pharynx					Remarks
			Congestion	Dropsy	Epithelium Ablution	Infiltration	Congestion	Haemorrhage	Dropsy	Epithelium Ablution Necrosis	Infiltration	
54	1	2	+++	+++	++	+				+		Necrosis found on epithelium of pharynx & part of arytenoid cartilage
80	1	11	+++	++		+	+++	+		+++	+	
84	2	16	+++	+	+++		+					
82	3	19	+++	+	±			++				
83	3	23	+++	+++				+	±			Haemorrhage observed on a part of chorda vocalis spuriae
85	3	23	+++	±			/	/	/	/	/	
81	4	23	+++	+			+++	+++		±		
56	8	26	+++				++	++	+		±	
71	11	38.5	+++				+	+				
79	13	52.5	+++	+	+		/	/	/	/	/	
75	14	54.5	+++	+	+			+				
73	14	57.5	+++				++		+			

Incl 1, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE II HISTOLOGICAL OBSERVATION OF TRACHEA AND LARYNX (CONT'D)

51	22	79	+++	±	±	+	+					Haemorrhage observed on connective tissue around pharynx
72	23	84	+++				++		++			
63	24	88	+++				++	+	+	+++	++	
61	24	89	+++				+			+++		Necrosis found on mucous membrane of pharynx
58	25	92	+	+	+		+++	+	+	+++	++	
65	25	96	+				/	/	/	/	/	

NOTE: +, ++, and +++ are only arbitrarily selected by the authors to indicate the relative extent of the pathological changes. / indicates no examination.

Incl 1, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

THE INFLUENCE OF THE ROCK POWDER USED IN THE COAL MINES UPON THE HUMAN BODY

By

Tadatoshi MIYAZAKI and Goro NIWA
Pathological Research Laboratory, Mitsui Medical Institute for Industry of Mitsui Mining Co., Ltd., Fukuoka-ken

ABSTRACT

Unpublished Report

The present experiment pertains to the influence exerted by the rock powder upon the human health. The experiment was conducted over an extended period from July 1940 to April 1944. The rock powder employed in this experiment was of the same type as that used in the Miike Coal Mine of Mitsui Mining Co., Ltd.

1. Experimental Method and Materials:

a. Test animals: For the present experiment 22 mature rabbits and 33 guinea pigs were employed.

b. Rock powder: Cottrell dust was obtained from the Miike Power Plant.

(1) Chemical composition and pH value of the dust were as follows:

Chemical Component	SiO_2	Free SiO_2	Al_2O_3	Fe_2O_3	CaO	MgO	SO_3	CO_2	Na_2O
Distribution, %	39.93	12.15	17.30	10.54	15.52	1.51	2.96	0.17	2.23

pH = 10.4

(2) Size of the rock powder: The sieving test of the rock powder with the standard sieve gave the following distribution:

Grain Size, mesh	< 100	100-200	200-300	> 300
Distibution, %	10.7	15.9	22.7	50.7

Incl 2, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

(3) Shape of the rock powder: Nearly all grains were found to be spherical in shape.

c. Dust Inhalation Method and its Duration: All the test animals were placed in the dust inhalation box described in the previous report (Igaku to Seibutsugaku, 11, No. 4, 235-239 (1947)). The animals were made to inhale as much rock powder as possible for 5 to 8 hours daily except Sundays and holidays until all the animals died.

The duration of the experiment and the period of inhalation were as follows:

Animal	Rabbits	Guinea Pigs
Duration of experiment	16-1107 days	1-262 days
Period of inhalation	75-6293 hours	6-1698 hours

2. Experimental Results:

The histological observations of the trachea, larynx and the lungs were made on both the test animals, rabbit and guinea pig. The results are summarized in Tables I, II, III, and IV.

The pathological changes noted in the experiment are as follows:

a. Acute or sub-acute laryngitis and trachitis were witnessed in all the test animals.

b. In the early stages, the lungs showed bronchitis, dropsy, localized haemorrhage, emphysema, atelectasis, catarrhal pneumonia, engorgement, etc. Pulmonary abscess often appeared in the later stages. When macroscopically examined, the rock powder deposit appeared as slab-colored or blackish miliary or extra-miliary linear macules beneath the pleura and also the pulmonary sections. The appearance of these spots was particularly pronounced in the rabbits after 920 hours of dust inhalation and in the guinea pigs after 255 hours. The presence of the cells which had ingested appreciable amount of rock powder was detected in 200 hours in the rabbits by examination under the microscope, but they appeared from the beginning in the case of the guinea pigs. These macroscopically visible spots of rock powder deposits were collections of several pulmonary alveoli in which dust cells that had ingested large amount of the minute rock powder were settled. Before these spots appeared, idio-lobular (special lobular) pulmonary apex foci consisting of rock powder ingested cells had come into existence. The

existence of both the spots and the pulmonary apex foci mentioned above grew more distinct in rabbits after the 1173 hour. From around the 2000th hour, they began to spread diffusively over the entire lung area bringing about a widely disseminated aletectitic condition. Such a diffusive type of pathological changes appeared in guinea pigs from around the 1400th hour. Such a proliferation of the connective tissues, as typically seen in the case of silicosis, was not witnessed in the present experiment.

c. The lymphatic gland of the pulmonary hilus showed the deposition of rock powder in rabbits after 166 hours and in guinea pigs after 58 hours, and it was seen to grow steadily in size as the time progressed. The proliferation of the lymphatic glands were often observed. In the rabbit that had inhaled dust particles for 5776 hours, the proliferation had assumed the form of mediastinal tumor.

d. A slight myocardiac deterioration and localized infiltration of small round cells often appeared in the heart of the rabbits from around the 1000th hour, but no such distinct pathological changes appeared in the guinea pigs.

e. The spleen underwent no particularly pronounced pathological changes except for atrophy of the lymphoglandular tubercles and the haemosiderosis and atrophy of the splenic medullae. Only in one case, amyloid processes was observed.

f. The engorgement and atrophy of the liver cells were witnessed in the liver and when the experiment was conducted over a longer period, abscess and biliary duct inflammation appeared in a few cases.

g. The kidney, as a rule, showed no marked pathological changes.

As the pathological changes were produced under specially intensified experimental conditions, the authors are not justified to use them without modifications as a yardstick in determining the hazardness of rock powder in the coal mines to the human health.

TABLE I - HISTOLOGICAL OBSERVATION OF RABBIT LUNGS

Animal No.	Duration of Experiment days	Period of Inhalation, hours	Congestion	Haemorrhage	Dropsy	Atelectase	Emphysema of the Lungs	Bronchitis	Catarrhalic pneumonia	Abscess Formation	Change in Bronchus & Blood Vessel Peripheral	Connective Tissue Proliferation	Pleurisy	Existence of Rock Powder Cell: Single (Few rock powder devoured)	Existence of Rock Powder Cell: Diffused (Few rock powder devoured)	Existence of Rock Powder Cell: Tubercle Formation	Existence of Rock Powder Cell: Pulmonary Hilus Lympha
86	16	75.0	x		xx	x	x	x									
87	20	166.6	x			x	x	x									x
111	31	196.5	xx		xx	x		x						x			x
110	32	204.0	x		x	x	xx	xx		x	x		x	x			xx
88	34	208.0	x	x		xxx	xx	x			xx			x			x
107	42	261.5	xx		x			x						x			
104	51	345.0	x			x	x	x			x			x			xx
103	63	357.2	xx		x	x	xx	x	x	x	x			x			
106	80	528.0		x			x	x									x
108	107	628.0	x		xx	x	x	x			xx			x		x	xx
91	150	920.2	x		xx		x	xx			x			x		x	xx
90	167	1003.5	xx			x		x						x		x	xx
92	169	1013.2	xx		xx	xx	xx	xx	xx	xx	xx			x		xx	x
93	191	1173.2				x	xx	x	x		x	x		xx		xx	xx
89	207	1294.5	x			x		x						x		xx	xx
97	274	1928.7	x		xx			xx	x		xx			xx	x	xx	x
94	315	1985.2	xxx		xx			xxx			xx	xx		xx	x	xxx	xx
99	344	2214.7	xx		x	x	x	x				xx		xx	x	xxx	x
95	380	2347.7				x	x	x		xx				xx	x	xxx	x
96	415	2587.7	x			x	x	x		xxx		xx		x	x	xxx	xx
109	1013	5776.9					x	x	xx	xxx				xx	x	xxx	
102	1103	6283.9			x	xx	xx	xx			xx	xxx		xx	xx	xxx	xx

NOTE: x, xx and xxx are only arbitarily selected by the authors to indicate the relative extent of the pathclogical changes

TABLE II - HISTOLOGICAL OBSERVATION OF RABBIT TRACHEA AND LARYNX

Animal No.	Duration of Experiment, days	Period of Inhalation, hours	Observation of Trachea				Observation of Larynx				
			Congestion	Dropsy	Epithelium Ablution	Infiltration	Congestion	Haemorrage	Dropsy	Epithelium Ablution	Infiltration
86	16	75.0									
87	25	166.6	xx		x					x	
111	31	196 5			x	x				x	xx
110	32	204.0									
88	34	208.0	x		x		x			xx	xx
107	42	261.5			x	xx				x	x
104	51	345.0	x	x	x		x		x	xx	
103	63	357.2	x		xx	x	x		x	x	
106	86	528.0	xxx		xx	x	xx			x	x
108	107	628.0	xx		x	x				x	x
91	150	920.2	xxx		x					x	x
90	167	1003.5			x	x		xx		x	
92	169	1013.2			x	x			xx		xx
93	191	1173.2	xxx	xx	x	x					x
89	207	1294.5	xxx							x	x
97	274	1928.7	x	x	x		z	z	z	z	z
94	315	1985.2	xxx	x	xx		z	z	z	z	z
99	344	2214.7		x	x		x			x	x
95	380	2347.7			x	x				x	xx
96	415	2587.7	z	z	z	z				x	
109	1013	5776.9									
102	1103	6283.9	z	z	z	z	z	z	z	z	z

NOTE: x (see Table 1)
z denotes no prominent changes

Incl 2 Report TID, GHQ, FEC APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

TABLE III - HISTOLOGICAL OBSERVATION OF GUINEA PIG
TRACHEA AND LARYNX

Animal No.	Duration of Experiment, days	Period of Inhalation hours	Observation of Trachea: Congestion	Dropsy	Epithelium Ablution	Infiltration	Observation of Larynx: Congestion	Haemorrhage	Dropsy	Epithelium Ablution	Infiltration
22	1	6.2			x		x			x	x
23	1	6.2	x		x					x	
24	1	6.2	x		x					x	x
25	1	6.2			xx						
26	1	6.2	x		x	x					
13	3	16.0			x	x					
14	11	58.0	x		xx	x	xx		x	x	xx
15	11	58.0	x		x	x	x				x
17	13	58.4		x	x						x
19	14	67.4	xx		x	xx	x			x	
20	14	67.4			x	x			x		x
21	14	67.4	xx		x	x	x			x	x
28	14	79.2			x	xx	x			x	
37	15	86.5	x		x	xx	x				x
38	22	126.5			x	x					
48	22	144.0	xx		x	xx					
34	38	234.2	x		xx	x					
36	38	234.2	xx	x	xx	x	x			x	x
49	39	241.5		x	xx	x				xx	
33	41	246.7	x		x	x			x	x	xx
32	39	248.7	xx		x	x	x			xx	
35	39	248.7	x		x						
27	41	255.7	xx		x	x			x	x	
29	41	255.7	x			x					
30	44	255.7			x	x					
31	44	255.7			x	xx					
40	54	379.0			x	x					
41	59	418.0		x		x					
42	59	418.0	xx		x	x					
43	59	418.0			x	x					x
44	59	418.0	xx		x	x					
47	236	1440.5	x		xx				x	xx	
46	262	1698.0	xx		xxx	x				xx	xx

NOTE: See Table I

TABLE IV - HISTOLOGICAL OBSERVATION
OF GUINEA PIG LUNGS

i- l .	Duration of Experiment, days	Period of Inhalation, hours	Congestion	Dropsy	Atelectase	Emphysema of Lungs	Bronchitis	Catarrhalic Pneumonia	Tubercle Lymph	Change in Bronchus & Blood Vessel Periphery	Existence of Rock Powder Cells: Single (a)	Diffused (a)	Tubercle Formation (b)	Pulmonary Hilus Lympha
2	1	6.2	x		x		x	x		x	x			
3	1	6.2	x	x	x	x	x	x		x	xx			
4	1	6.2	x		x		xx				xx			
5	1	6.2	x	x			xx	x	xx	xx	x			
6	1	6.2	x	x			x	xx			x			
3	3	16.0	x				xxx			x	x			
4	11	58.0	x	x			xx	x	x	xx	x			
5	11	58.0					x	xx	xx		xx			
7	13	58.4	x		x	x	x	xx		x	xx			x
9	14	67.4	xxx		xx		xx	x			xx			
0	14	67.4				x	xx				xx			
1	14	67.4	x		x	x	x				x			
3	14	79.2			x		x	x	xxx	xxx	x			x
7	15	86.5	xx	x	xx			x		x	x			
[illegible]	22	126.5					x				xxx			x
3	22	144.0							xx	x	x			
4	38	234.2	x		xx	x	x	xx			x			
6	38	234.2		xx				x			x		x	
9	39	241.5	x		x	x	x			x	x		x	
3	41	246.7	x		x						x			
2	39	248.7	x	x			xx	xx		x	x			
5	39	248.7			xx		xx	xx	x		x			x
7	41	255.7			x			x			x		x	
)	41	255.7	x	x			xx	xx		x	x			
)	44	255.7	x		x	x	x	xx		x			x	
1	44	255.7	xx				x	xx			x		x	
)	54	379.0	x								x		x	x
1	59	418.0			x	x	x	x	xx		xx		x	xx
2	59	418.0	x			x	xx			x	xx		x	
3	59	418.0	x		xx		x	xx		x	xx			
4	59	418.0	xx		xx		x	x	xx	x	xx		x	
7	236	1440.5	x					x			xx	xx	xx	x
5	262	1658.0			x			x	x	xxx	xx	xx	xx	

'E: (a) Few rock powder devoured (b) Rock powder definitely devoured
Others, see Table I

EXPERIMENTAL STUDIES OF THE INFLUENCES OF TEXTILE FIBERS
ON THE LUNGS OF RABBITS AND THE DEVELOPMENT OF TUBERCULOSIS

By

Dr. Hideichi ODA

Institute of Hygiene and 2nd Medical Clinic,
Faculty of Medicine, Kyushu University, Fukuoka

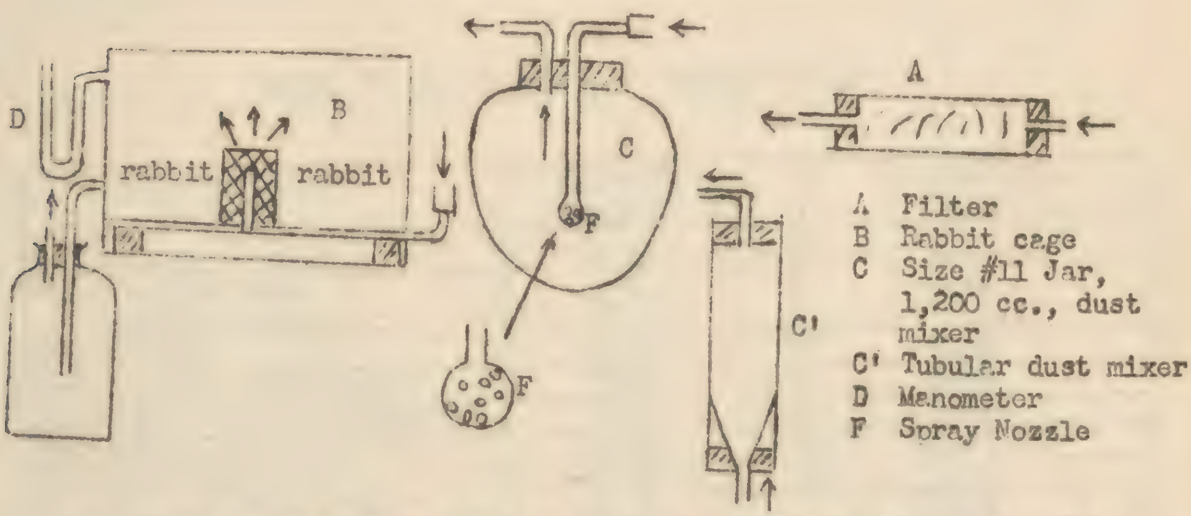
ABSTRACT

(Published in Fukuoka Medical Journal (Japan), 36, 511-542 (1943))

Little has been known concerning the different types of injuries incurred to the lungs by the inhalation of organic fiber particles. The author studied the pathological relation between pneumoconiosis and the tubercular changes by conducting experiments with rabbits by allowing them to inhale various kinds of fiber dust.

The experimental procedure consisted in keeping groups of 5 to 6 rabbits of medium weight in wooden cages for 2 hours each day over a period of 10 to 120 days. Air laden with fiber dust was admitted into these cages with a pump and the circulation of the fiber dust was conducted by air current through a glass vessel (Size #11 Jar), which was later replaced by an improved glass cylinder of 60 cm long and 7 cm in diameter.

Apparatus:



The fiber dusts were cleaned as much as possible and were found to consist of short cut wool, cotton and cellulose threads. The percent distribution by length of cotton, wool and staple fibers are tabulated in Table I.

Incl 3, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE I PERCENTAGE DISTRIBUTION BY LENGTH OF DIFFERENT FIBER DUST

Length, μ	Fiber Dust					
	Cotton %		Wool %		Staple Fiber %	
Below 11	3.1		3.3		2.2	
12-22	5.1		5.7		4.1	
23-33	3.7		4.8		5.6	
34-44	4.0		3.1		3.4	
45-55	1.4	33.7	1.5	39.3	1.0	34.2
56-66	2.3		2.6		2.3	
67-77	1.4		1.8		1.1	
78-88	1.5		2.2		2.0	
89-99	1.2		1.0		0.7	
100-110	10.0		13.3		11.8	
111-220	18.1		16.5		16.9	
221-330	10.1		11.8		9.2	
331-440	13.1		10.9		12.2	
441-550	11.0		10.5		12.1	
Over 550	14.1		11.0		15.1	

The ash content of weaving fiber were analyzed and found to be as indicated in Table II.

TABLE II ASH CONTENT OF WEAVING FIBER

Kind of Fiber Material	Moisture Content, %	Ash Content, %
Raw cotton (Brazil)	7.28	2.30
Waste cotton under Carding machine	5.90	5.75
Cotton yarn	7.71	1.18
Experimental cotton dust	7.19	0.98
Absorbent cotton, commercial	7.56	0.15
Raw wool (Australia)	10.86	24.82
Coarse woolen yarn	12.83	0.71
Experimental wool dust	13.47	0.66
Staple fiber	12.66	0.21
Experimental staple fiber dust	12.39	0.19

After the dust laden air was inhaled by the rabbits for 10 to 120 days, some were killed for examination of the pathological changes in their lungs while the remainder were contaminated with tubercle bacilli of bovine type by subcutaneous injection. After the injection of the bacteria, the animals were allowed to inhale fiber dusts for another 15 days and were killed 55 days later. Their lungs and other organs were prepared for anatomical examination.

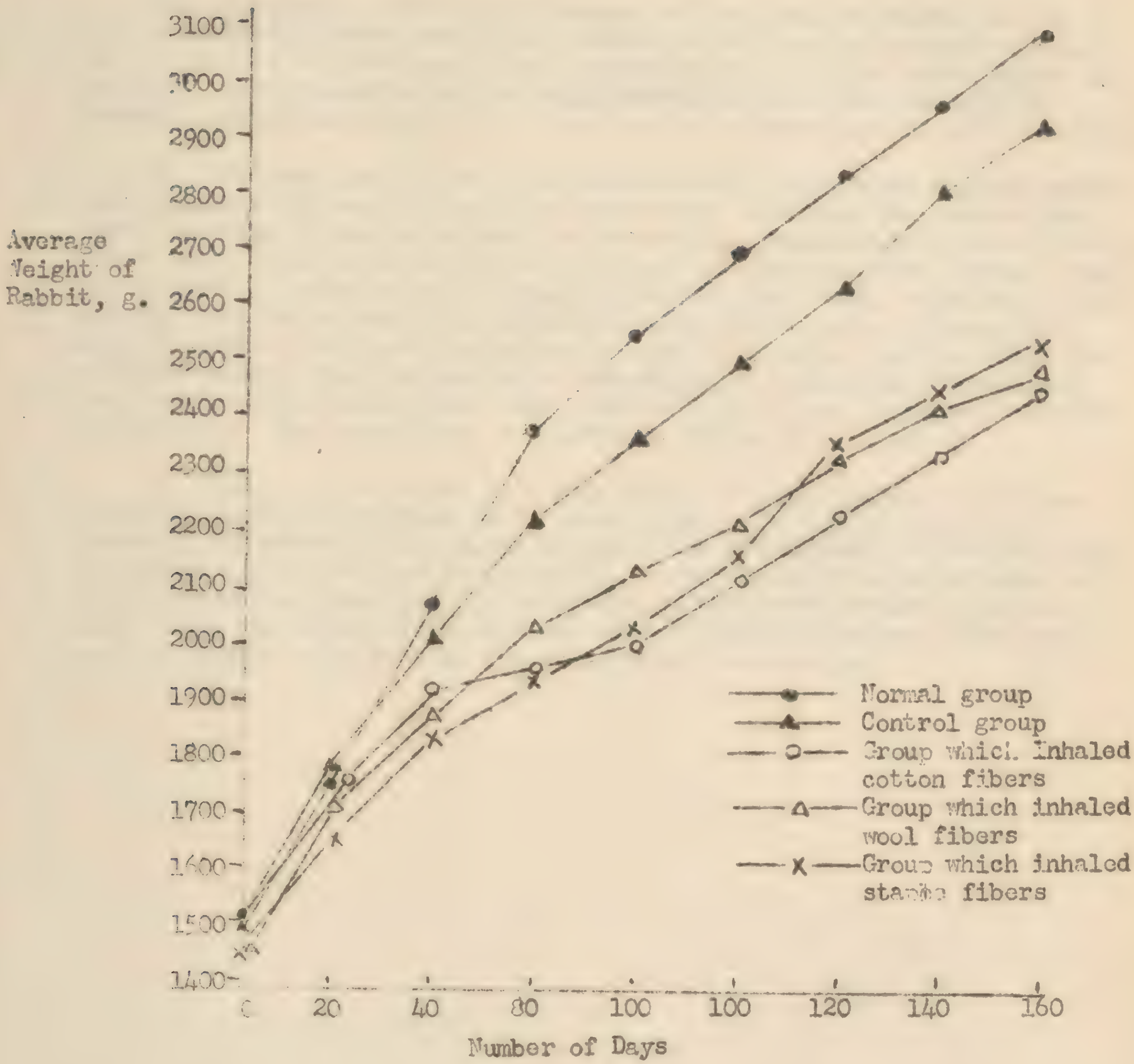
Conclusions: The results of the examination can be summarized as follows:

a. It was noted that the inhaled fiber dusts exerted harmful influences upon the subsequent growth of the animals as indicated in Table 3 and graphically represented in Figure 1.

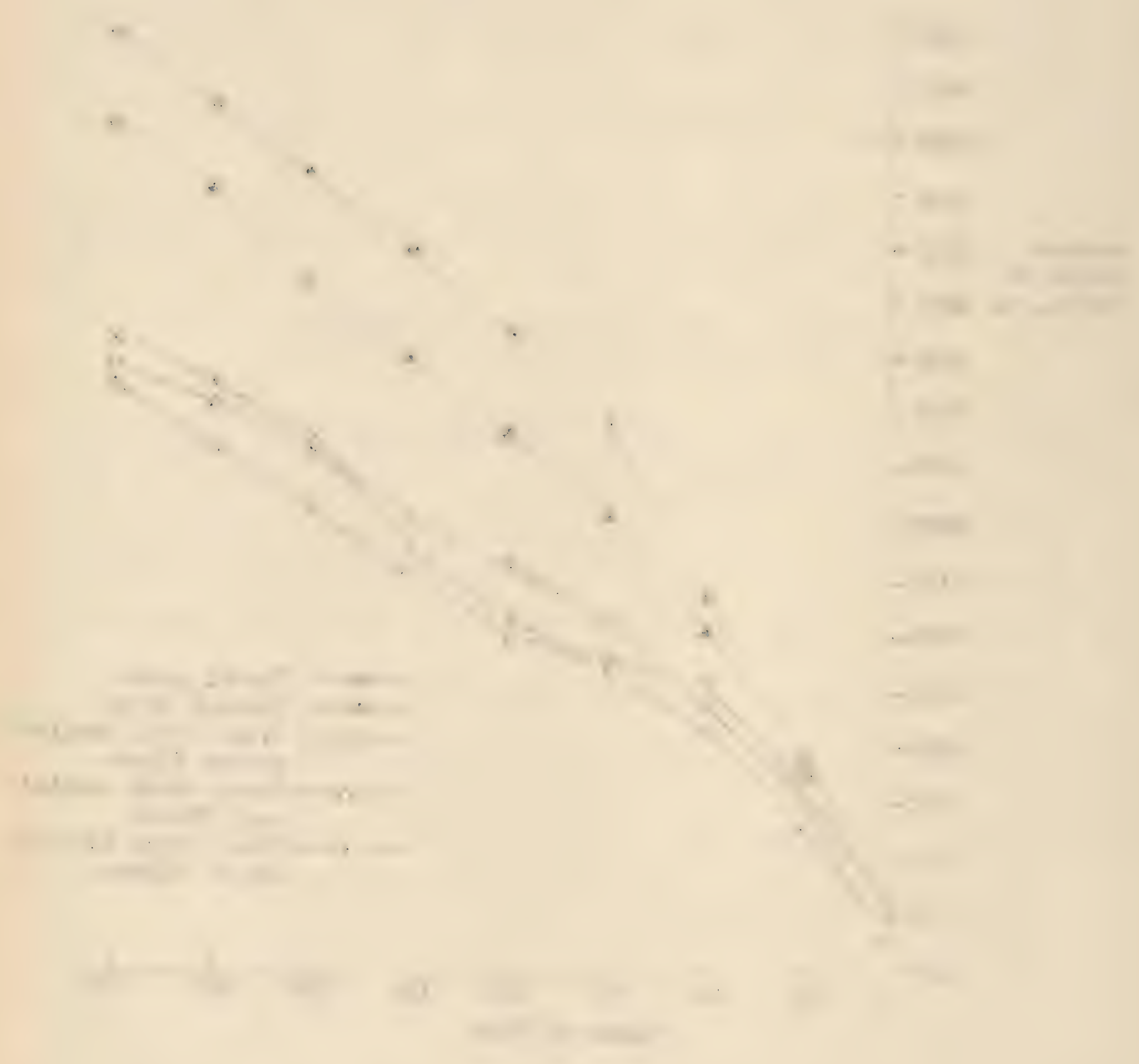
TABLE III INCREASE IN WEIGHT OF RABBITS
DURING THE EXPERIMENT (CONDENSATION OF 5 TABLES)

Number of Rabbits and Kind of Dust Fiber Inhaled	Average Weight of Rabbit, g.								
	At time of Inhalation	20 days	40 days	60 days	80 days	100 days	120 days	150 days	160 days
3-Normal	1476	1753	2063	2360	2530	2683	2820	2963	3090
4-Control	1503	1765	2003	2200	2338	2478	2608	2780	2905
6-Cotton Fiber	1512	1757	1912	1950	2002	2114	2220	2336	2447
6-Wool Fiber	1470	1752	1892	2025	2123	2218	2320	2410	2497
6-Staple Fiber	1450	1665	1820	1927	2033	2148	2347	2443	2533

FIGURE 1 - GRAPHICAL REPRESENTATION OF THE INCREASE IN WEIGHT OF RABBITS DURING THE EXPERIMENT



Incl 3, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48



b. The fibers filtered deep into the alveoli by normal breathing and injured the lung tissues, which showed atelectasis, namely, vicarious emphysema, but no proliferation of the connective tissues was noted.

c. Pronounced pathological changes of the lungs consisted in the more or less diffusive knot-like bleeding which appeared macroscopically on the surface and sectional face, microscopically in the parenchymas, and somewhat less pronounced in the neighborhood of the blood vessels and bronchi. Often the fibers were found in the surroundings of the hemorrhage.

d. The dust inhaled and the tubercle bacilli injected animals showed more numerous dilated tubercle foci than those that did not inhale fiber dust. Further it was noted that in the case of animals that inhaled cotton fiber dust, their pathological changes were of more exudative nature. But in the case of animals that inhaled cellulose fiber dust, which were less harmful than the others, the pathological changes of these tuberculars were as mild as the dust controlled or normal animals. Compared with the affected lungs, other organs which were directly exposed to fiber dust, even the harmful cotton fiber dust, underwent far less pronounced tubercular changes. The results are tabulated in Tables IV, V, and VI.

e. Thus, it is evident that the lesion of lungs caused by the continuous inhalation of fiber dust, even in slight and mild degree, was proved to be powerful inducement to wards the development of tuberculosis. The results are tabulated in Table VII. From the above observations, the author concluded that with the exception of the least harmful cellulose fiber dust, all types of fiber dust, even if their injurious effect may vary in degree, make it easy for tuberculosis to develop.

TABLE IV GROUP WHICH INHALED COTTON FIBER DUST

Duration of Inhalation	Rabbit No.	Period and Number of Times of Inhalation	Slaughtered date	Weight		Bleeding of Lung Surface		Bleeding of Sliced Surface		Grade of Congestion		Emphysema		Phenomenon of Pleura	Swelling of Lymphatic Gland of Pulmonary hilus
				Beginning of Inhalation, g.	At Slaughtered Time, g.	Left	Right	Left	Right	Left	Right	Left	Right		
Short Period	2	1/5-10/5 10 times in 10 days	10/5	1580	1690	-	-	+	+	±	±	+	+	-	-
	5	"	"	1490	1600	++	++	+	+	-	±	-	-	-	-
	9	1/8-12/8 10 times in 12 days	12/8	1500	1600	-	-	-	-	-	+	-	-	-	-
Long Period (A)	1	1/5-20/8 100 times in 112 days	20/8	1500	2170	+++	+++	++	+++	+++	+++	+	++	-	-
	3	1/5-30/7 81 times in 91 days	30/7	1430	1970	++	+	-	+	+	+	+	+	air vesicle	-
	4	1/5-20/8 100 times in 112 days	20/8	1450	2210	-	-	-	-	±	±	++	++	-	-
Long Period (B)	6	"	19.10	1640	2420	++	++	+++	+++	+	++	+++	+++	air vesicle	
	7	12/5-20/8 90 times in 101 days	"	1540	2600	-	-	-	-	+	++	+	++	-	-
	8	"	"	1510	2510	-	+	+	+	+	+	+	++	-	-

NOTE: TODA's Standard Tuberculin Reaction Reading

- \- Negative, no culture
- ∓ Semi-negative, 1-4 mm.
- ± Semi-positive, 5-9 mm.
- \+ Weakly positive, 10-14 mm.
- ++ Medium positive, 15-19 mm.
- +++ Positive, 20-30 mm.
- ++++ Strongly positive, Over 31 mm and formation of air vesicles.

Incl 3, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

[illegible]

[illegible]

− Negative, no reaction

± [illegible], 1-4 mm.

± [illegible], 5-9 mm.

+ Weakly positive, 10-[illegible] mm.

++ [illegible]

+++ [illegible]

++++ [illegible], Over [illegible]

[illegible]

[illegible] "[illegible] of Inoculation of [illegible] Preparations" [illegible]

TABLE V GROUP WHICH INHALED WOOL FIBER DUST

Duration of Inhalation	Rabbit No.	Period and Number of Times of Inhalation	Slaughtered Date	Weight: Beginning of Inhalation, g.	Weight: At Slaughtered Time, g.	Bleeding of Lung Surface: Left	Bleeding of Lung Surface: Right	Bleeding of Sliced Surface: Left	Bleeding of Sliced Surface: Right	Grade of Congestion: Left	Grade of Congestion: Right	Emphysema: Left	Emphysema: Right	Phenomenon of Pleura	Swelling of Lymphatic Gland of Pulmonary hilus
Short Period	K 1	24/11-3/12 10 times in 10 days	3/12	1500	1620	+	+	+	+	±	-	++	++	-	-
	K 2	13/12-24/12 10 times in 12 days	24/12	1500	1610	-	-	-	-	-	-	+	+	-	-
	K 3	"	"	1510	1600	-	-	-	-	-	-	-	±	±	-
Long Period (A)	11	25/8-12/12 100 times in 110 days	12/12	1420	2220	++	+++	++	+++	+	+	+++	+++	-	-
	12	25/8-22/11 81 times in 90 days	22/11	1470	2130	-	-	-	+	+	+	+++	+++	-	-
	14	25/8-12/12 100 times in 110 days	12/12	1580	2390	-	-	-	-	++	++	+++	+++	-	-
Long Period (B)	10	"	10/2	1450	2570	-	-	-	-	-	-	++	++	Gray macula Air Vesicle	-
	13	"	"	1500	2530	-	++	+	+	±	±	++	++	-	-
	15	"	"	1400	2610	-	-	-	-	-	-	+	+	-	-

NOTE: TODA's Standard Tuberculin Reaction Readings Used, See Table IV.

TABLE VII GROUP WHICH INHALED STAPLE FIBER DUST

Rabbit No.	Period and Number of Times of Inhalation	Slaughtered Date	Weight: Beginning of Inhalation, g.	Weight: at Slaughtered Time, g.	Bleeding of Lung Surface: Left	Bleeding of Lung Surface: Right	Bleeding of Sliced Surface: Left	Bleeding of Sliced Surface: Right	Grade of Congestion: Left	Grade of Congestion: Right	Emphysema: Left	Emphysema: Right	Phenomenon of Pleura	Swelling of Lymphatic Gland of Pulmonary hilus
K 4	24/11-3/12 10 times in 10 days	3/12	1500	1590	+	-	-	-	++	+	-	-	-	-
K 5	13/12-24/12 10 times in 12 days	24/12	1510	1620	-	-	-	-	-	-	-	-	-	-
K 6	"	"	1500	1570	+++	+++	++	++	+	+	-	-	-	-
17	25/8-22/11 81 times in 90 days	22/11	1480	2160	-	+	+	+	+	++	+	+	-	-
20	25/8-12/12 100 times in 110 days	12/12	1400	2120	-	+	-	+	-	±	++	++	-	-
21	"	"	1400	2300	-	-	-	-	-	±	++	++	-	-
16	"	10/2	1460	2530	-	+	-	++	±	+	±	+	-	-
18	"	"	1500	2660	-	-	-	-	+	+	-	+	Air vesicle grey macula	-
19	"	"	1430	2660	-	-	-	-	-	+	+	++	Air vesicle	-

NOTE: TODA's Standard Tuberculin Reaction Readings Used, See Table IV.

TABLE VII TUBERCULAR CHANGE OCCURRED IN RABBITS WHICH INHALED FIBER DUST

Group	Rabbit No.	Weight at beginning of inhalation, g.	Period and Number of Time of Inhalation: Prior to Innoculation	Period and Number of Time of Inhalation: After Innoculation	Weight at the time of Innoculation	Slaughtering Date	Weight at the time of Slaughtering, g.	Weight of Lung, g.	Bleeding of Lung Surface: Left	Bleeding of Lung Surface: Right	Tubercular Change: Left Lung	Tubercular Change: Right Lung	Tubercular Change: Liver	Tubercular Change: Spleen	Tubercular Change: Kidney	Swelling of Pulmonary hilus
Normal	1	1490	-	-	2000	25/6	2360	28	-	-	+	+	-	-	+	-
	2	1470	-	-	2060	26/6	2460	24	-	-	+	+	-	-	+	+
Control	1	1400	22/3-1/5 39	2/5-12/5 14	1900	25/6	2380	32	-	-	+	+	-	-	-	-
	2	1370	"	"	1860	26/6	2320	36	-	-	++	++	-	-	+	+
Inhaled Cotton Fiber	1	1660	"	"	2150	"	2320	45	+	++	++	+++	-	-	+	+
	2	1820	"	"	2200	27/6	2520	40	++	+	++	++	-	-	++	+
	3	1670	"	"	2100	"	2000	65	+	+	++++	++++	-	-	+++	++
Inhaled Cotton Fiber	4	1520	18/3-1/5 40	"	2000	"	2050	60	+	++	++++	++++	++	++	+++	++
Inhaled Staple Fiber	5	1420	"	"	1870	26/6	1975	38	-	-	++	++	-	-	+++	-
	6	1570	"	"	2100	27/6	1900	30	-	-	+++	+++	-	-	+	++
	7	1390	"	"	1800	"	2170	31	-	-	+	+	-	-	+	-
	8	1420	"	"	1920	"	2200	27	-	-	++	++	-	-	+	+
	9	1450	"	"	1900	26/6	2300	25	-	-	+	++	-	-	+	++

NOTE: TODA's Standard Tuberculin Reaction Reading

- − Negative, no culture
- ∓ Semi-negative, 1-4 mm
- ± Semi-positive, 5-9 mm
- + Weakly positive, 10-14 mm
- ++ Medium positive, 15-19 mm
- +++ Positive, 20-30 mm
- ++++ Strongly positive, Over 31 mm and formation of air vesicles

EXPERIMENTAL STUDY ON THE CORRELATION BETWEEN SILICOSIS AND PULMONARY TUBERCULOSIS

by

Dr. Itsuo KURODA

Post Graduate Student, Institute of Hygiene,
Faculty of Medicine, Kyushu University, Fukuoka.

ABSTRACT from Unpublished Report

Using the experimental materials and procedures mentioned below, the author, as a student of hygiene, has conducted a series of experiments to determine the correlation between silicosis and pulmonary tuberculosis. The results of the experiments are as follows:

1. Experimental Materials.

a. Silica dusts

Fine red and white silica dusts, which were brownish red in color, were collected from the edge mill and tube mill of the refractory brick plant of Yawata Iron Works. Approximately 90% of the particles were smaller than 5μ in size. Under examination with a Nicol microscope, the particles consisted of two types, light brownish and colorless transparency, with both presenting fractured appearances. The light brownish particles were somewhat larger in size embodying brownish granules, while the colorless transparent particles, larger in number than the former, were flat in shape with somewhat rugged edges. Their sectional surface gave glassy luster and was homogenous in quality. Their refraction of light was comparatively pronounced in direct light, but in the case of larger particles the extinction of light was pronounced. Their chemical composition was reported by the analysis section of the Yawata Irom Works laboratory as follows:

Composition in % / Dusts	SiO_2	Al_2O_3	Fe_2O_3	CaO	MgO	MnO	S	P_2O_5	C
Edge Mill	93.12	2.07	1.89	0.18	0.98	0.06	0.02	0.11	0.12
Tube Mill	89.96	2.88	2.04	0.62	1.54	0.18	0.08	0.06	0.75

b. Tubercle bacilli.

The bacilli were supplied from the stock of the tubercle bacilli of bovine type kept by the Department of Bacteriology, Kyushu University. The bacteria was accurately weighed and placed into sterilized physiological solution so that 1 ml. of solution contained 1 mg.

c. Test Animals.

White mice, each weighing 70-80 grams were used for the experiment.

2. Experimental Procedures

The experiment was conducted by using the apparatuses and procedures designated by Dr. ODA, Professor of Hygiene (Refer to Fukuoka Medical Journal (Japan), 36, 511-542 (1943), Inclosure 3).

The silica dusts were first thoroughly dried in an electric dessicator and then approximately 140-150 grams of the dust were blown into the test box for a period of 1 hour. The blower is capable of blowing in 66 liters of air/min, thus, the concentration of dust particles in the test box was approximately 275 mg/liter of air.

After the test animals were made to inhale the silica dust for an hour every other day and for a required length of time, they were killed for examination.

The animals were contaminated with tubercle bacilli by injecting 0.3-0.5 ml. of the tubercle solution into the nape subcutaneously.

Upon killing the animals a microscopic examination of their lungs was conducted and the the lung specimens were immersed in 10% formalin solution and preserved in paraffin. They were then treated by haematoxylin-eosin double dyeing and von Giesen dyeing.

When the dust particles were blown into the test box, the white mice became restless and began running around the box almost immediately or within a period of 2 minutes at the latest and rubbing their noses with their forelegs in an effort to evade the inhalation of the dust particles. In 5 to 7 minutes, the mice quieted down.

The test animals were divided into 5 groups, each consisting of 10 mice.

Group 1: The annimals were made to inhale silica dust particles once every other day for a total of 57 inhalations. Then the animals were examined to determine the extent their body weight and lungs were affected by the inhalation of silica dust particles.

Group 2: Air alone was admitted into the test box instead of silica dust contaminated air for a total of 42 inhalations. Then the animals were given subcutaneous injection of tubercle bacilli solution followed by inhalation of air for 15 times. The animals were examined to determine the effect of the tubercle injection upon their body weight and lungs.

Group 3: The animals were treated in the same manner as above except that after the injection of tubercle bacilli, silica dust contaminated air was blown into the test box instead of air.

Group 4: The animals were made to inhale silica dust particles every other day for 42 inhalations and then subcutaneous tubercule injections were given. After the injection, air alone was blown in for 15 inhalations and the same examinations as before were conducted.

Group 5: The animals were treated in the same manner as above except that silica dust contaminated air was inhaled in place of air after the injection of tubercle bacilli.

3. <u>Experimental Results</u>:

a. <u>Effect of the Inhaled Silica Dust Particles and Tubercle Bacilli Injection upon the Weight of the Animals</u>

The animals were weighed weekly and the mean values, (in grams), are tabulated as follows:

	Number of Weeks															
Group	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	-10	-15	-10	-3	3	10	15	22	30	36	40	45	48	52	57	62
2	10	18	28	35	45	53	62	72	80	85	92	97	93	90	88	85
3	9	20	26	39	47	57	68	75	82	87	93	98	92	87	80	75
4	-14	-17	-12	-6	4	8	14	20	27	34	41	46	42	40	37	33
5	-16	-18	-9	-5	2	7	13	18	28	35	42	48	40	36	32	23

With continued inhalation of silica dust particles, the animals suffered loss of weight for the first 2 weeks, but after that they gradually regained their weight. The injection of tubercle bacilli solution decreased the weight of the animals.

b. Examination of the Lungs

Group 1: The lungs were light brown in color. The tissues were hardened and revealed the presence of small bleeding blotches, both new and old. Numerous pearl-like white granules were observed with unaided eyes. Some localized tubercular colonies of infiltrated round cells were present in the neighborhood of the bronchi and blood vessels upon histological examination. The pulmonary alveolar septa was partially infiltrated with diffusive round cells and proliferated. The pulmonary alveoli were slightly dilated, disintegrated, and fused with one another to become emphysematous and linked with one another to form networks. The bronchial epithelial cells were proliferated to a pronounced extent or partially desquamated. Pronounced engorgement of the capillary blood vessels of the pulmonary alveolar septa and bleeding of the interstitial substances were often observed. On the alveolar septa and in the parts infiltrated with lymphocells were found sporadic existence of silica dust cells. The connective tissues were proliferated in the colonies of the localized tubercular infiltrated round cells and also in the parts infiltrated with diffusive lymphocells.

Group 2: The lungs of the animals of Group 2 appeared grayish-white in color, and showed sporadic existence of millet-sized tubercules, but no haemorrhagic blotches were detedted when macroscopically examined. The glands of the pulmonary hilus were swollen to the size of sharp pen point. A small number of isolated peculiar tubercular colonies were found present when histologically examined. Small number of diffusive round cells were found infiltrated around the bronchi, blood vessels, and in the pulmonary alveolar septa. The pulmonary alveoli were clean and no emphysematous changes were detected.

Group 3: Macroscopic examination of the lungs of the animals of Group 3 gave similar results as those of Group 1. Instead of the white pearl-like granules, greyish white millet-sized tubercles were sporadically present. The glands of the pulmonary hilus were swollen to the size of a pen point. The infiltration of the localized tubercular round cells was not so pronounced, but small colonies of isolated peculiar tubercular type were sporadically present when histologically examined. The pulmonary alveolar septa were proliferated with the infiltration of diffusive round cells and were partially atelectasic and mostly emphysematous. The engorgement of the capillary blood vessels and the haemorrhage of the intercellular substances were pronounced. The bronchial epithelial cells were either considerably swollen or desquamated. Sporadic presence of silica dust particles were detected.

Group 4: The macroscopic examination of the lungs of animals in Group 4 were about the same as in Group 1. However, the small bleeding blotches present were all old and no fresh ones were present. Whitish gray tubercles of millet size were sporadically present. The existence of the localized tubercular round cell infiltration was pronounced around the blood vessels and the bronchi. The connective tissues were also highly

proliferated. The same kind of pathological process, as occurred in Group 3, were also detected in Group 4, but in a slightly minor degree.

Group 5: The macroscopic examination of the animals in Group 5 were about the same as in Group 4, but numerous small bleeding blotches, both new and old, were sporadically present. The same pathological processes, as seen in Groups 3 and 4, were also detected to a more pronounced extent when histologically examined.

4. Conclusions

Summarizing the results of the experiments, the author came to the following conclusions:

1. The silica dust particles inhaled by the animals specifically affected the lungs by giving rise to various pathological processes and the physical vitality of the animal was affected by causing loss of weight or retarding the increase in weight.

2. The subcutaneous injection of tubercle bacilli solution brings about tuberculosis and causes loss of weight.

3. When silica dust particles are inhaled into the lungs which were previously contaminated with tubercle bacilli, tuberculosis is aggravated and causes considerable loss in weight.

4. If the animal contracted tuberculosis after continuous inhalation of silica dust particles, the pulmonary tuberculosis does not undergo any pronounced progress nor is any loss of weight incurred provided further inhalation of silica dust particles is not made.

5. When continued inhalation of silica dust particles is followed by contamination of tubercle bacilli and then the inhalation of the dust is resumed, the pulmonary tuberculosis undergoes a further marked development with considerable loss of weight.

6. The appearance of small bleeding blotches in the lungs and the loss in weight as a result of the inhalation of silica dust particles weakened the vitality of the animal. Thus, it decreased the resistance against diseases, both locally and generally, making it possible for tuberculosis to develop, or making it worse if tuberculosis already existed.

undifferentiated. The same kind of pathological process, as occurred in group 3, were also detected in group 4, but in a slightly minor degree.

Group 5: The macroscopic examination of the animals in Group 5 [illegible] the same as in Group 4, but numerous small bleeding blotches, both new and old, were sporadically present. The same pathological processes, as that in Groups 3 and 4, were also detected to a more pronounced extent [illegible].

4. Conclusion

Summarizing the results of the experiments, the author came to the following conclusions:

1. The silica dust particles inhaled by the animals specifically affected the lungs by giving rise to various pathological processes and the physical vitality of the animal was affected by causing loss of weight or retarding the increase in weight.

2. The [illegible] injection of tubercle bacilli [illegible] brings about tuberculosis and causes loss of weight.

3. When silica dust particles are inhaled into the lungs which were previously contaminated with tubercle bacilli, tuberculosis is aggravated and causes considerable loss in weight.

4. If the animal contracted tuberculosis after continuous inhalation of silica dust particles, the pulmonary tuberculosis does not undergo any pronounced progress nor is any loss of weight incurred provided further inhalation of silica dust particles is not made.

5. When continued inhalation of silica dust particles is followed by contamination of tubercle bacilli [illegible] the inhalation of the dust is resumed, the pulmonary tuberculosis undergoes a further marked development with considerable loss of weight.

6. The appearance of small bleeding blotches in the lungs and the loss in weight as a result of the inhalation of silica dust particles weakened the vitality of the animal. Thus, it decreased the resistance [illegible] disease, [illegible] generally, making it possible for tuberculosis to develop, or making it worse if tuberculosis [illegible] ready [illegible].

[illegible] D 000 [illegible] 600. Subject: "Locus of Inspection of [illegible] in [illegible]"

DISCHARGING PROCESS AND THE EXPELLING VELOCITY
OF INHALED DUST IN THE TRACHEA

By

Seisaburo NAGATANI, Department of Hygiene,
Faculty of Medicine, Kyoto University, Kyoto

ABSTRACT

(Published in National Hygiene (Japan), 7, 436-454 (1932))

Introduction:

In the past HASH (1925), HILL (1927), UMEDA (1929), etc. have conducted measurement on the dust velocity in the trachea due to ciliary motion, but certain physiological conditions and methods of conducting the experiment were not satisfactory. The author suggests that the trachea must be extracted from the body and kept at the proper body temperature of the test animal. The extracted trachea must be kept upright. The mucous membrane must be kept in a saturated state by periodically dipping the extracted trachea in Ringer's solution to prevent dehydration. The atmospheric air must be circulated over the surface to assimilate as nearly as possible the conditions in the human body. With this in mind, the author commenced the experimental studies on the extracted trachea of oxes.

Experimental Apparatus:

Figure 1A shows a thermostat equipped with an automatic thermocontroller and a thick glass front door which has four holes, c, to correspond with the side arm, c', of the glass tube. The hole, k, (3 cm diameter), on the top of the thermostat is closed with a stopper, k', which holds the air and gas tubes. Two thermometers are set in the thermostat; one at the top and the other at the bottom of the apparatus near the front door. Figure 1B shows a glass tube 7 cm diameter and 20 cm long with the open end closed with a cork stopper through which a thermometer and a glass tubing, g, are inserted. There are two projecting side arms, c', of 0.5 cm diameter on the side of glass tube, b. These holes are used for intaking or exhausting the air or gasses, for dipping the test piece into the Ringer's solution and for placing of the dust particles onto the extracted trachea suspended in the tube.

Preparation for Experiment and Procedures:

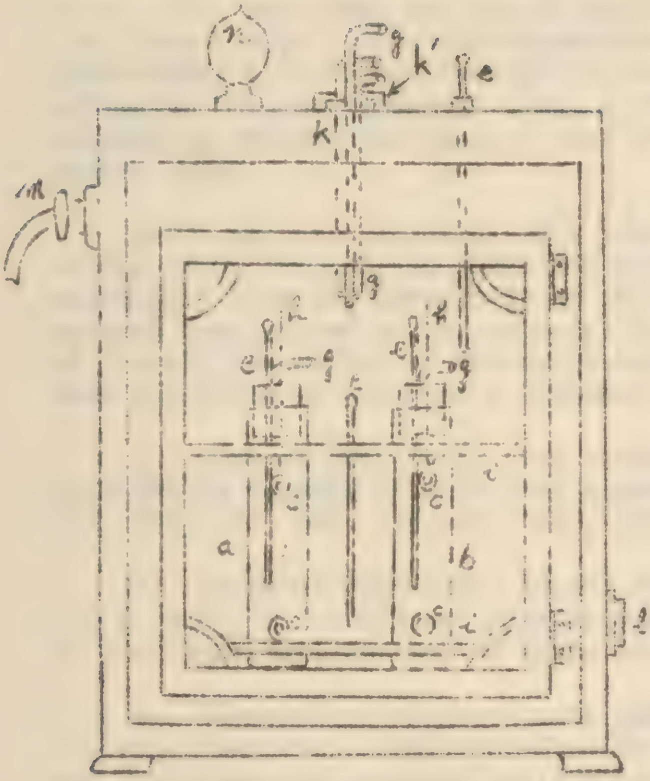
a. Material: Trachea of the ox was extracted within 24 hours after slaughtering and used after necessary preparations.

b. Preparation of the Extracted Trachea: The mucous membrane of the trachea was washed with Ringer's solution to remove the foreign matters. The material was then cut lengthwise in strips 15 cm wide and a paper

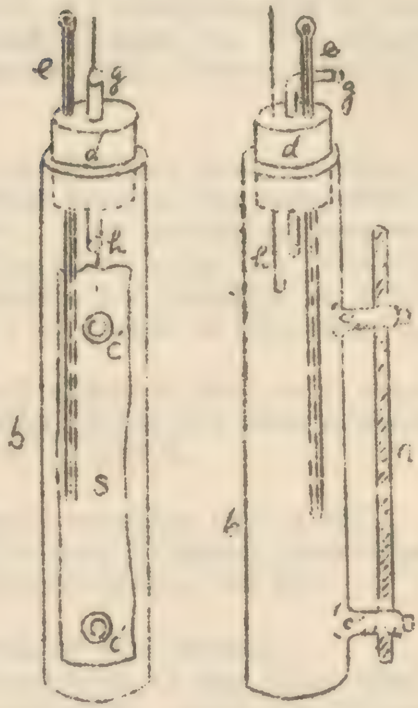
Incl 5, Report TID, GHQ FEC APO 500 Subject: "Locus of Impaction of Particulates", dated 15 Dec 48

Figure 1

A. Thermostat



B. Glass tubes in which to set test materials



Front View   Side View

a Glass door
b Glass tube
c Holes in door
c' Projected parts
d Cork stopper
e Thermometer
g Glass pipe
h Hook
i Pipe supporter
k Hole of 3 cm diameter
k' Stopper
l Automatic thermo-controller
m Wire
n Light
s Test material

..pe 1 mm wide, which was marked at every centimeter, was fixed onto the center of the mucous membrane from top to bottom as a marker. The trachea, thus prepared, was suspended on a hook, h, in the glass tube, b, so that approximately 1 cm of the lower portion was dipped in the Ringer's solution. The glass tube was set in the thermostat maintained at 38°C for more than 1 hour. When the temperature reached 38°C in the tube, the glass tube, g, inserted through the stopper, d, was connected by rubber tubing to the corresponding tube, g, through stopper, k. The side arm projecting through the hole, c, was connected with a rubber tubing to a vacuum pump.

Moist air at a velocity of 1 L/hr. was admitted from the upper part of the glass tube, b, in which the extracted trachea was suspended and discharged from the lower hole of the tube. Dust particles (charcoal powder) were placed on the material from the lower hole, c'. The velocity of the ciliary motion of the extracted trachea was measured by timing the dust particles to traverse a distance of 1 cm marked on the paper tape.

c. Size of Dust Used: Ten samples of charcoal dust were prepared by shifting through Tyler's test sieves with equivalent mesh numbers 325, 270, 230, 200, 170, 140, 120, 100, 70, 35 and 8.

d. Ringer's Solution: Normal Ringer's solution (8.0 g NaCl, 0.2 g $CaCl_2$, 0.2 g KCl and distilled H_2O to make 1 liter) prescribed by the Veterinary Section of Kyoto Prefectural Office was used.

e. Temperature of the Mucous Membrane of the Trachea: The experiment was conducted after the atmosphere in the glass tube, b, and the thermostat reached equilibrium temperature, which is the same temperature as the extracted trachea, so that normal reaction of the ciliary movement could be obtained

Experimental Results:

The dust expelling velocity of extracted ox trachea due to the tracheal ciliary motion was measured by using charcoal dust powder ranging 0.074-0.088 mm in diameter (Mesh No. 5) at different time intervals. The results are tabulated in Table I.

[illegible] 1 cm wide, which was marked at every centimeter, was fixed onto the surface of the mucous membrane from top to bottom as a marker. The trachea, thus prepared, was suspended on a hook, h, in the glass tube, b, so that approximately 1 cm of the lower portion was dipped in the Ringer's solution. The glass tube was set in the thermostat maintained at 38°C for more than 1 hour. When the temperature reached 38°C in the tube, the glass tube, c, inserted through the stopper, d, was connected by rubber tubing to the corresponding tube, g, through stopper, k. The tube [illegible] projecting through the hole, e, was connected with a rubber tubing to a [illegible] pump.

Moist air at a velocity of 1 L/hr. was admitted from the upper part of the glass tube, b, in which the extracted trachea was suspended and discharged from the lower hole of the tube. Dust particles [charcoal powder] were placed on the extracted [illegible]. The velocity of the ciliary motion of the extracted trachea was measured by timing the dust particles to traverse a distance of 1 cm marked on the paper tape.

c. Size of Dust Used: Ten samples of charcoal dust were prepared by shifting through Tyler's test sieves with equivalent mesh numbers [illegible], 42 and 5.

d. Ringer's Solution: Normal Ringer's solution (8.0 g NaCl, 0.2 g CaCl2, 0.2 g KCl and distilled H_2O to make 1 liter) prescribed by the Veterinary Section of Kyoto Prefectural Office was used.

e. Temperature of the Mucous Membrane of the Trachea:
The experiment was conducted after the atmosphere in the glass tube, b, and the thermostat reached equilibrium temperature, which is the same temperature as the extracted trachea, so that normal reaction of the ciliary movement could be obtained.

Experimental Results:

The dust expelling velocity of extracted ox trachea due to the tracheal ciliary motion was measured by using charcoal dust powder ranging 0.0[illegible]–0.[illegible] mm in diameter (Mesh No. 5) at different time intervals. The results are tabulated in Table I.

Incl 5, Report TID, GHQ FEC, APO 500 Subject: "Loess of Imposition of [illegible]", dated 15 Dec 48

TABLE I RELATIONSHIP BETWEEN DUST EXPELLING VELOCITY AND ELAPSE OF TIME

Extracted Trachea Sample No.	Dust Expelling Velocity (mm/sec) of Extracted Trachea After Elapse of Time.							
	5 min.	10 min.	30 min.	1 hour	2 hours	5 hours	10 hours	15 hours
I	0.833	0.909	1.000	0.909	0.909	0.909	0.909	0.833
II	0.769	0.833	0.667	0.714	0.769	0.769	0.714	0.667
III	0.714	0.714	0.667	0.667	0.625	0.714	0.625	0.625
IV	0.667	0.714	0.714	0.625	0.625	0.625	0.667	0.714
V	0.625	0.555	0.588	0.555	0.625	0.555	0.555	0.555
VI	0.555	0.555	0.555	0.526	0.500	0.555	0.526	0.555

There is no appreciable decrease in the velocity of the ciliary action within 15 hours after slaughtering if the trachea is maintained in the thermostat at 38°C.

2. The dust expelling velocity of different areas of the trachea was conducted by taking samples from known distances below the glottal rim. As shown in Table II, the difference of velocity does not depend upon the different surface area of the trachea.

TABLE II RELATIONSHIP BETWEEN THE DUST EXPELLING VELOCITY AND THE DIFFERENT SURFACE AREA OF THE TRACHEA.

Extracted Trachea Sample No	Dust Expelling Velocity (mm/sec) of Extracted Trachea with respect to Samples Taken from Known Distances below the Glottal Rim							
	5 cm	10 cm	15 cm	20 cm	25 cm	30 cm	35 cm	40 cm
I	0.833	1.000	0.833	1.000	0.909	0.909	0.909	0.769
II	0.769	0.769	0.667	0.667	0.714	0.667	0.667	0.769
III	0.714	0.714	0.714	0.667	0.625	0.625	0.667	0.667
IV	0.625	0.667	0.667	0.625	0.625	0.625	0.625	0.625
V	0.625	0.588	0.555	0.625	0.555	0.625	0.555	0.555
VI	0.555	0.555	0.555	0.588	0.526	0.526	0.555	0.526

3. The dust expelling velocity depends upon the different parts of the trachea, but no appreciable difference in the velocity was observed for the same test piece with respect to the size of the dust particles. The results of the dust expelling velocity for 10 dust sizes upon 6 extracted trachea samples are tabulated in Table III.

TABLE III RELATIONSHIP BETWEEN THE DUST EXPELLING VELOCITY AND THE SIZE OF THE DUST PARTICLES.

Size of Sieve Number	Dust Particles Diameter Size mm	Dust Expelling Velocity (mm/sec) of Extracted Trachea from Various Areas.					
		I	II	III	IV	V	VI
1	less than 0.043	0.833	0.769	0.714	0.667	0.588	0.625
2	0.043-0.053	0.833	0.714	0.667	0.667	0.625	0.526
3	0.053-0.061	1.000	0.667	0.625	0.588	0.588	0.526
4	0.061-0.074	0.769	0.669	0.667	0.667	0.555	0.555
5	0.074-0.088	0.714	0.714	0.667	0.667	0.625	0.500
6	0.088-0.104	0.909	0.714	0.588	0.667	0.625	0.588
7	0.014-0.147	0.769	0.714	0.625	0.667	0.625	0.555
8	0.147-0.208	0.833	0.667	0.625	0.625	0.625	0.555
9	0.208-0.495	0.833	0.714	0.625	0.667	0.625	0.555
10	0.495-0.991	0.833	0.714	0.625	0.667	0.625	0.555

4. The dust expelling velocity was made with respect to shape, hardness specific gravity of dust particles, such as cork, charcoal, coal, sand, glass, zinc, iron, brass, copper, and lead powders. The results are tabulated in Table IV. The velocity of the dust particles depends upon the surface of the trachea from which the sample was taken but not upon the shape, hardness and specific gravity of the dust.

TABLE IV RELATIONSHIP BETWEEN THE DUST EXPELLING VELOCITY AND THE SPECIFIC GRAVITY OF THE DUST PARTICLES.

Type of Dust Particles	Specific Gravity	Dust Expelling Velocity (mm/sec) of Extracted Trachea from Various Areas					
		I	II	III	IV	V	VI
Cork powder	0.22-0.26	0.909	0.714	0.714	0.667	0.555	0.588
Charcoal dust	0.35-0.60	0.769	0.769	0.769	0.625	0.588	0.588
Coal dust	1.20-1.50	0.769	0.769	0.769	0.625	0.555	0.526
Fine Sand	2.51-3.10	1.000	0.909	0.667	0.625	0.526	0.526
Powdered glass	6.86-7.24	0.909	0.833	0.667	0.667	0.555	0.555
Zinc powder	7.60-7.80	0.833	0.833	0.769	0.667	0.588	0.526
Iron powder	8.32	0.833	0.833	0.714	0.714	0.588	0.500
Brass powder	7.73-8.79	0.909	0.909	0.714	0.667	0.526	0.588
Copper powder	8.93	1.000	0.769	0.714	0.667	0.588	0.555
Lead powder	11.43	0.909	0.769	0.833	0.667	0.588	0.555

Conclusions:

1. The dust expelling velocity of various types of dust particles were measured on the extracted trachea of ox in an experimental apparatus thermostatically maintained at 38°C.

2. The dust particles travelled vertically at a constant velocity parallel with the marker.

3. Apparently no decrease in the dust expelling velocity of the dust particles was observed with the excess amount of mucus secreted by the mucous membrane. The different dust particles were effectively wrapped by the mucus and transported towards the top of the extracted trachea.

4. The change in the dust expelling velocity can not be observed with freshly extracted trachea maintained at 38°C within the first 15 hours.

5. The difference in the dust expelling velocity of dust particles at different parts of the extracted trachea can not be observed as far as the same test piece is concerned.

6. No difference in the dust expelling velocity can be observed with regard to the physical properties of dust, such as size, shape, hardness and specific gravity.

COMPARATIVE STUDY OF DUST
EXPELLING VELOCITY OF TRACHEA OF VARIOUS
SPECIES OF ANIMALS

By

Dr. Masanobu SAITO, Department of Hygiene,
Faculty of Medicine, Kyoto University, Kyoto.

ABSTRACT

(Published in National Hygiene (Japan), 9, 395-406 (1934))

Introduction:

Many research reports have already been published regarding the dust expelling action of the trachea due to the ciliary motion of of the respiratory tract in the animals.

In experiments with prisoner's bodies immediately after their execution, HENKE (1896) discovered that coal dust attached to the tracheal mucuous membrane moved the width of the cartilage towards the larynx within 15 minutes. LOMMEL (1908) placed lycopocium on the tracheal mucuous membrane of the trachea extracted from a dog and measured the transitional and expelling velocity of the dust, which was found to be 0.033-0.04 mm/sec. GEBHARD (1909), in his experiment on the extracted trachea of a dog, determined the expelling velocity to be 0.4 mm/sec. with coal dust. HASCH (1925) injected a suspensiod of lycopodium stained with fuchsin into the small bronchus of dogs and measured the time required for the suspensiod to reach the operated hole. The mean value of the expelling velocity was found to be 0.076 mm/sec. HILL (1928) stretched extracted pieces of tracheal mucuous membrane from various species of mammals on cork plates, which were warmed by immersion in Ringer's solution maintained at 38°C, and dropped a suspensiodal solution of graphite or kaolin dust. The velocity of the particles was found to be 0.3-0.16 mm/sec. UMEDA carried out a similar experiment to HILL's by using neat's trachea, not seperated from the cartilage, on an inclined plane. The maximum velocity of 2.1 mm/sec. was obtained at small angle of inclination. NAGATANI previously reported that the dust expelling velocity of extracted trachea was 0.7 mm/sec for neats, 0.4 mm/sec for dogs and 0.2 mm/sec for rabbits. However, the report lacked physiological considerations and was not free from technical criticisms. Thus, the author made a comparative study of the dust expelling velocity of the trachea of warm blooded animals by using NAGATANI's improved apparatus and secured interesting results which are compiled in this paper.

Test Material and Experimental Procedures:

a. Animals used: The trachea of warm blooded animals, such as neats, horses, dogs, pigs, rabbits, monkeys, chickens, guinea pigs, and rats, were submitted to the experiment within 24 hours after slaughtering.

Incl 6, Report, TIP. GHQ, FEC, APO 500, Subject: "Locus of Impaction of Particulates" dated 15 Dec 48.

b. Foreign matter: The foreign substance used in this experiment was chiefly charcoal dust, which was sieved through Tyler's Nos. 325, 270, 200, 170, 140, 120, 100, 70, 35, and 18, classified into 10 grades of fineness. Dust particles sifted through sieve No. 140, size 0.074-0.088 mm dia., was the most predominant size used.

c. Apparatus and Procedure: (Refer to NAGATANI, National Hygiene, 7, 436-454 (1934)).

d. Experimental Temperature: The temperature of the extracted trachea during the experiment was maintained at the average body temperature of the respective animals as shown in Table I.

TABLE I EXPERIMENTAL TEMPERATURE

Animal	Temperature of Experiment, °C	Normal Body Temperature, °C
Neat	38	37.5-38.6
Horse	38	37.7-39.5
Dog	39	38.5-39.5
Pig	39	38.5-40
Rabbit	39	38.3-39.5
Monkey	37	- - -
Chicken and Turkey	42	41-42.5
Cat	38.2	38.5-39
Guinea pig	38.5	38-39
Rat	38.5	- - -

e. Conditions of Experiment: The experiment was conducted under saturated humidity and the dust expelling velocity was determined and compared by measuring the time required to transport the dust particle 1 cm distance.

Results of the Experiment:

The results of the experiment are tabulated in Tables II (summary of 11 tables), III and IV.

TABLE II DUST EXPELLING VELOCITY

Species	Maximum and Minimum Time Required to Transport Dust Particles 1 cm Distance (sec.)	Maximum and Minimum Velocity, (mm/sec)	Mean Value	
			Time (sec)	Velocity (mm/sec)
Goats	10-20	1.000-0.500	15	0.698
Horses	10-20	1.000-0.500	15.3	0.689
Pigs	35-50	0.286-0.200	41.6	0.243
Dogs	19-35	0.528-0.286	24.7	0.425
Cats	27-57	0.370-0.175	39.5	0.271
Monkeys	25-27	0.400-0.370	26	0.384
Rats	23-37	0.434-0.272	24.2	0.36
Turkeys	18-36	0.555-0.277	25.1	0.425
Chickens	13-21	0.769-0.476	17	0.588
Guinea pigs	[illegible]-120	- - - -	94	- - -
Rats	80-100	- - - -	89	- - -

TABLE III RELATIONSHIP BETWEEN DUST EXPELLING VELOCITY AND ELAPSE OF TIME

Animal Species	Dust Expelling Velocity, mm/sec with Elapse of Time						
	5 min.	10 min.	30 min.	1 hour	2 hours	3 hours	6 hours
Goats	0.833	0.833	0.833	0.769	0.833	0.769	0.833
Horses	0.526	0.500	0.500	0.500	0.526	0.500	0.500
Pigs	0.286	0.286	*	*	-	-	-
Dogs	0.416	0.416	0.312	*	*	-	-
Cats	0.250	0.250	0.200	0.250	0.250	*	*
Monkeys	0.370	0.370	0.370	0.370	0.370	0.370	-
Rabbits	0.312	0.312	0.372	*	*	-	-
Turkeys	0.458	0.458	0.277	*	*	-	-
Chickens	0.476	0.250	*	*	-	-	-
Guinea pigs	*	*	-	-	-	-	-
Rats	*	*	-	-	-	-	-

Notes: * Required 1 to 2 minutes for dust particles to move 1 cm.
* Required over 2 minutes for dust particles to move 1 cm.
- Cessation of movement.

TABLE IV-RELATIONSHIP BETWEEN DUST EXPELLING VELOCITY
AND THE SIZE OF DUST PARTICLES

Size of Dust Particles		Dust Expelling Velocity of Extracted Trachea, mm/sec										
Seive No.	Grain Size mm Dia.	Neats	Horses	Pigs	Dogs	Cats	Monkeys	Rabbits	Turkeys	Chickens	Guinea Pigs	Rats
1	0.043	0.833	0.652	0.286	0.500	0.312	0.384	0.400	0.476	0.526	*	*
2	0.043-0.053	0.833	0.652	0.272	0.526	0.312	0.384	0.416	0.476	0.526	*	*
3	0.053-0.061	1.000	0.652	0.286	0.500	0.312	0.384	0.416	0.476	0.500	*	*
4	0.061-0.074	0.769	0.526	0.286	0.500	0.312	0.384	0.370	0.500	0.476	*	*
5	0.074-0.088	0.714	0.555	0.286	0.500	0.312	0.348	0.416	0.476	0.526	*	*
6	0.088-0.108	0.909	0.588	0.272	0.416	0.250	0.370	0.400	0.458	0.476	*	*
7	0.108-0.147	0.769	0.555	0.222	0.286	0.200	0.370	0.333	0.400	0.526	*	*
8	0.147-0.208	0.833	0.555	0.200	0.200	*	0.312	0.250	0.458	0.416	-	-
9	0.208-0.495	0.833	0.555	*	*	*	0.277	*	0.476	0.286	-	-
10	0.495-0.991	0.833	0.555	-	-	-	0.181	-	0.476	0.222	-	-

NOTES: * Required 1 to 2 minutes for dust particles to move 1cm.
* Required over 2 minutes for dust particles to move 1cm.
.. Cessation of movement.

Incl 6, Report FID GHQ, FEC, APO 500, Subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

Conclusions:

The conclusions obtained from the results are as follows:

a. The dust expelling velocity of extracted trachea varies in the different specits of animals. The velocity was the greatest in the case of neats and horses and decreased in the following order: chickens, rabbits, dogs, turkeys, monkeys, cats, pigs, rats and guinea pigs. The data in Table II discloses that the larger trachea has greater expelling velocity, and that animals with long trachea, such as fowls, have comparatively large dust expelling velocity. This difference in the velocity is probably due to the difference in the length of the tracheal cilia and also by the influence exerted by the mucus.

b. By placing the tracheal specimens in a thermostat for a measured length of time in advance of the experiment, it was proved that the degree of retardation in the dust expelling velocity due to the elapsing of time varies with the vitality energy and durability of the epithelial cells in the respiratory duct of the respective animals.

c. The size of the dust particles was ascertained to have some influence upon the dust expelling velocity, though the degree of influence was not the same among the various species of animals. In the case of horses and neats, the size of the dust particles had no influence on the dust expelling velocity; while dust particles greater than 0.99 mm diameter could not be expelled in the pigs, and those larger than 0.20[illegible] mm diameter could not be transported by the cilia. (Refer to Table IV).

It is easily expected that the expelling velocity of dust particles in living animals is far more active, but there are no experimental method for its determination. However, this experiment with the extracted trachea suggests that the dust expelling ability of the living animals varies depending upon the species of animals.

INFLUENCE OF VARIOUS PHYSICO-
CHEMICAL CONDITIONS UPON DUST EXPELLING
FUNCTION OF TRACHEA

By

Seisaburo NAGATANI
Department of Hygiene, Faculty of Medicine,
Kyoto University, Kyoto

ABSTRACT

(Published in National Hygiene, 7, 645-714 (1932)

A. INTRODUCTION: The author previously reported (National Hygiene, Vol 7, pg 436) regarding the dust expelling velocity of an extracted neat trachea and the relationship between the velocity and the size, shape, hardness and specific gravity of the dust. The influence of various physico-chemical conditions on the dust expelling function of the trachea was conducted and reported in this paper, not only from the interest of physiological standpoint but also for the improvement of prophylactic as well as therapeutic measures of the respiratory diseases.

B. INFLUENCE OF TEMPERATURE UPON THE DUST EXPELLING ACTION OF THE TRACHEA

Experimental Procedure: Neat trachea, treated as previously reported, were hung in a glass cylinder which was placed in a thermostat after it was cooled at 50°C for an hour. The temperature of the thermostat was raised to 10, 15, 20, 25, 30, 38, 40, 42, and 45°C respectively. At each temperature the dust expelling velocity was measured by using charcoal dust, 0.074-0.088 mm in diameter, as the foreign substance.

Results of Experiment: The data obtained from the experiment are tabulated in Table I and II.

Conclusions:

1. The dust expelling velocity of an extracted neat's trachea is most active and endurable at 38°C (average body temperature) under saturated humidity. The velocity is more pronouncedly decreased when the temperature rises above this point than when it falls below this point. In other words, the dust expelling ability of the extracted trachea is more easily affected and deteriorated by the ascent of the temperature above 38°C than by its descent below this point.

2. The velocity decreasing ratio per 1°C is greater above 38°C than below this temperature.

3. The dust expelling action is suspended if the temperature is higher than 45°C or lower than 10°C. The dust expelling ability, thus suspended, can be revived, if the suspension is due to the fall of temperature from 10°C by raising the temperature. But if the expelling ability is suspended due to the rise of temperature beyond 45°C, the once lost ability could not be regained even if the trachea is cooled to its original temperature. Therefore, the suspension of expelling action due to the high temperature is caused by death of the ciliary cells.

C. INFLUENCE OF MEMBRANE HUMIDITY UPON THE DUST EXPELLING ACTION OF THE TRACHEA.

Since there are no previous records concerning the investigation of the relationship between the dust expelling action of the trachea and the humidity of the tracheal mucous membrane, the author conducted the following experiment.

Experimental Procedure: In order to vary the humidity of the mucous membrane in the trachea, the extracted trachea were exposed to air of different moisture content after treatment in Ringer's solution. The three types of air current were as follows: (1) dry air (dried over $CaCl_2$ and conc. H_2SO_4); (2) normal laboratory air; and (3) damp air. Each type of air current was introduced into a glass cylinder in which the extracted tracheal membrane was supported over a small quantity of Ringer's solution at the bottom. The humidity in the cylinder was measured with the wet and dry hygrometer after the air current was introduced into the cylinder for an hour. During the experiment, the velocity of the air current was controlled at 1 liter/min by means of a gasmeter. The observation and measurement of the dust expelling action was conducted for an hour (to obtain an average value) by using charcoal dust, 0.074-0.088 mm diameter, as the foreign substance.

Results of the Experiment: The results are tabulated in Table III. The figures in parenthesis indicate the relative value of the respective velocities based upon the velocity measured before the introduction of the wet or dry air current to be 100.

Conclusions: The dust expelling ability was most effectively maintained in wet air and rapidly weakened in dry air. This fact indicates that the dust expelling action was performed by the mucous flow and that any excessive mucous which covered the cilia and the epithelial cells served not only to prevent it from becoming dry but also protection against irritations. Furthermore, it was disclosed that the expelling velocity is temporarily accelerated when the membrane is exposed to the air current. However, it is not clear as to whether this acceleration or revival was due to the chemical reaction of oxygen or carbon dioxide gas in the air or by the mechanical stimulation of the air current.

D. INFLUENCE OF RINGER'S SOLUTION MODIFIED WITH ACID, ALKALIES, COMMON SALT, AND GLUCOSE UPON DUST EXPELLING ABILITY OF THE TRACHEA.

Experimental Procedures: Various kinds of Ringer's solution were prepared for the experiment by varying the common salt content or glucose content and also by adding hydrochloric acid, sodium hydroxide or sodium bicarbonate into the solution. The solution thus prepared were called special Ringer's solutions to distinguish it from the ordinary Ringer's solution.

The test materials of the experiment were the freshly extracted neat trachea which had been kept in the air current of saturated humidity, temperature of 38°C and moistened periodically with Ringer's solution. The experiment was conducted by placing charcoal dust, 0.074-0.88 mm diameter, upon the mucous membrane of the trachea and the dust expelling velocity was measured repeatedly to secure an average value. The treatment of the trachea with special Ringer's solution was made by spraying with an injector for three minutes. After observing the dust expelling velocity for an hour, the trachea was washed several times with Ringer's solution and its dust expelling velocity was examined for an hour to determine the restoration power.

Results of the Experiment:

1. The effect of Special Ringer's solution prepared by using common salt are tabulated in Table IV. The indications of the signs used in the table are as follows:

a. Figures in parenthesis represent the relative values of the respective velocity prior to the application of special Ringer's solution.

b. (*) The dust expelling velocity was 0.167-0.083 mm/sec; i.e., it required one to two minutes for the dust particles to move 1 cm.

(*) The dust expelling velocity was below 0.083 mm/sec; i.e., it required more than two minutes for the dust particles to move 1 cm.

c. The hours or minutes written in the last column indicates the time which elapsed after the restoration process.

2. The effect of Special Ringer's solution prepared by mixing glucose are tabulated in Table V. The experiments were performed by using 5 kinds of special Ringer's solution prepared by mixing 1, 3, 5, 10, and 25% of glucose, respectively. When the concentration of glucose was either 1, 3, or 5%, the trachea was moistened at intervals of an hour with glucose solution for 5 hours, the trachea was then washed with normal Ringer's solution and the restoration change in the expelling ability was subsequently observed. When the concentration was either 10 or 25%, the special solution was applied for an hour then the restoration process observed for an hour.

3. The effect of basic and acidic Ringer's solution on the dust expelling velocity are tabulated in Tables VI, VII, and VIII.

Conclusions: By comparing the effects of various kinds of special Ringer's solution, the author obtained the following conclusions: Alkalies exert greater influence than acids on the dust expelling action of neat trachea, as shown in Table IX. Sodium bicarbonate which is far weaker in alkalinity than sodium hydroxide gives a more pronounced expelling effect than hydrochloric acid, if the comparison is made under appropriate consideration of their degree of ionization.

E. INFLUENCE OF VARIOUS CHEMICALS UPON DUST EXPELLING VELOCITY OF THE TRACHEA.

The author attempted to make clear the influence of adrenalin, atropine sulfate, pyrocarphine hydrochloride, cocaine hydrochloride, ammonia, formalin, acetone, creosote, camphor and menthol on the dust expelling velocity of the trachea extracted from neats by using Ringer's solution of these chemicals in various concentrations.

Experimental Procedures: The chemicals used in this experiment were Merck products of reagent quality. Each of these chemicals were dissolved and mixed with Ringer's solution. Each solution (38°C) was applied for 3 minutes to the extracted trachea which was kept at 38°C and under moisture saturated air current with its lower end dipped in Ringer's solution.

Camphor and menthol were applied in the vapor form either by conducting warm air through a 250 cc bottle containing 20 grams of camphor or menthol and introduced into the glass by cylinders in which contained the suspended trachea or by suspending a cotton gauze bag containing 10 gram of camphor or menthol parallel to the trachea in the cylinder. The author discriminated between the two cases by calling the former to be under vapor current and the latter to be in vapor atmosphere.

Results of the Experiment: The results of the experiment are tabulated in Tables X, XI, XII, XIII, XIV, XV, XVI, XVII, XVIII, XIX, XX, and XXI.

Conclusions: The author reached the following conclusions after surveying the results of the experiments.

a. Influence of chemical upon the original dust expelling velocity was as follows:

(1) No influence was observable when the applied chemical was either of the following: 0.1% adrenalin, 0.5% morphine hydrochloride, 0.1% cocaine hydrochloride, 0.00001% ammonia and 0.3% acetone solution.

(2) Only retarding effect was observed when the chemical was either of the following: 0.01-0.5% atrophine sulfate, 0.1-0.5% physostigmine salicylate, 5% morphine hydrochloride, 10% cocaine hydrochloride, 0.00005-0.001% ammonia, 0.001% formalin, 5-10% acetone, 0.1 and 0.5% creosote, saturated solution of camphor and its 0.5, 0.3 and 0.2 dilutions, 10% camphor-oil; saturated menthol solution.

(3) The velocity was accelerated at first and then slowed down by the following chemicals: 1% and 3% morphine hydrochloride, 0.3-5% cocaine hydrochloride, 0.00003% ammonia, 0.0001-0.0005% formalin solution, 1-3% acetone, 0.5, 0.2 and 0.1 dilution of menthol solutions.

b. The influence of the chemicals on the restoration of dust expelling ability once interrupted was as follows:

(1) The ability for restoration was most pronounced when the applied chemicals was either of the following: 0.01-0.5% atropine sulfate, 0.1-0.5% physostigmine salicylate, 1-3% morphine hydrochloride, 0.3-1% cocaine hydrochloride, 0.00003-0.00005% ammonia, 0.0001% formalin, 0.01-0.1% creosote, 0.3, 0.2, and 0.1 dilution of saturated camphor solution, 0.5 and 0.1 dilution of saturated menthol solution.

(2) The restoration was difficult when the chemical was either of the following: 5% morphine sulfate, 3-10% cocaine hydrochloride, 0.0001-0.001% ammonia, 0.0003-0.001% formalin, 3-10% acetone, 0.3-0.5% creosote, saturated camphor solution, 10% camphor-olive oil.

TABLE I RELATION BETWEEN TEMPERATURE AND DUST EXPELLING VELOCITY

Velocity / Temperature °C	below 10	10	15	20	25	30	35	38	40	42	43	45
Time Required to Move 1 cm	B(-)	B(*)	43'10"	6'22"	1'47"	43"	25"	15"	19"	22"	40"	B(*)
mm/sec.	B(-)	B(*)	0.00046	0.0026	0.009	0.023	0.040	0.667	0.526	0.435	0.250	B(*)
Percentage to the Velocity at 38°C.	B(-)	B(*)	0.6	4	14	35	60	100	79	65	37	B(*)

NOTES: B(-) indicates non-expellant action; B(*) indicates hardly visible action.

TABLE II DECREMENT RATIO OF DUST EXPELLING VELOCITY

Temperature °C	below 10	10-15	15-20	20-25	25-30	30-35	35-38	38-40	40-42	42-43	43-43
Difference in Percentage (of the Velocity at Individual Temperature to the Velocity at 38°C)	0	0.6	3.4	10	21	25	40	21	14	28	37
Velocity Decrement Ratio per 1°C	0	0.12	0.7	2	4.2	5	13.3	10.5	7	28	18.5
Percentage to the Maximum Decrement Ratio	0	0.4	2.5	7	15	18	47.5	37.5	25	100	66
Order of Velocity Decrement Ratio	XI	X	IX	VIII	VII	VI	III	IV	V	I	II

Incl 7, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE III RELATION BETWEEN DUST EXPELLING VELOCITY AND HUMIDITY OF MUCOUS MEMBRANE

Humidity	Velocity Prior to Application mm/sec.	Time Elapsed (min.) and Dust Expelling Velocity (mm/sec)				
		5'	10'	15'	30'	60'
Dry current	0.588	0.625(106)	0.625(106)	0.555(94)	0.435(74)	0.278(47)
Moderately Wet Current	0.769	0.769(100)	0.833(108)	0.833(108)	0.714(93)	0.667(87)
Saturated Wet Current	0.769	0.769(100)	0.833(108)	0.833(108)	0.769(100)	0.769(100)
Saturated Atmosphere Without Current	0.769	0.769(100)	0.769(100)	0.769(100)	0.769(100)	0.769(100)

NOTE: Figures in parenthesis indicates the relative percentage of dust expelling velocity to initial velocity.

TABLE IV RELATION BETWEEN DUST EXPELLING VELOCITY AND CONCENTRATION OF COMMON SALT

Concentration, %	Velocity before Application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec.)						Recovery and Remarks
		5'	10'	15'	30'	45'	60'	
Distilled water	0.667	0.667(11)	0.076(11)	0.111(17)	0.238(36)	0.357(53)	0.435(65)	The velocity before the application was regained in 60 minutes.
0.8	0.667	0.667(100)	0.667(100)	0.667(100)	0.667(100)	0.667(100)	0.667(100)	Velocity was constant during 24 hours.
1	0.667	0.667(100)	0.714(107)	0.714(107)	0.714(107)	0.714(107)	0.769(115)	Velocity was decreased after 2 hours.
3	0.667	0.200(30	0.333(50)	0.417(62)	0.454(68)	0.476(71)	0.588(88)	The velocity before the application was not restored after 1 hour.

TABLE IV (CONT'D)

5	0.714	(-)	(-)	(-)	0.2[illegible]	0.294(41)	0.322(47)	same as above
10	0.714	(-)	(-)	(-)	(-)	(±)	(*)	same as above

NOTES: (-) Dust expelling action suspected
(*) Dust expelling action 0.167-0.083 mm/sec
(±) Dust expelling action -0 083 mm/sec

TABLE V RELATION BETWEEN CONCENTRATION OF GLUCOSE AND DUST EXPELLING VELOCITY

Concentration, %	Velocity before application, mm/sec	Time (min.) and Dust Expelling Velocity (mm/sec)											Recovery and remarks
		3'	5'	10'	15'	30'	45'	60'	1°5'	2°	3°	5°	
1	0.667	0.714 (107)	0.714 (107)	0.769 (115)	0.769 (115)	0.714 (107)	0.769 (115)	0.769 (115)	0.714 (107)	0.714 (107)	0.714 (107)	0.667 (100)	Velocity is constant
3	0.588	0.667 (113)	0.714 (121)	0.769 (131)	0.769 (131)	0.769 (131)	0.833 (142)	0.833 (142)	0.769 (131)	0.714 (121)	0.667 (113)	0.625 (125)	The original velocity was regained 5 minutes later
5	0.667	0.769 (115)	0.833 (125)	1.000 (150)	1.000 (150)	1.000 (150)	1.000 (150)	1.000 (150)	0.909 (136)	0.909 (136)	0.909 (136)	0.833 (125)	The acceleration was still continued even 5 minutes after
10	0.667	0.175 (26)	0.185 (28)	0.175 (26)	0.227 (24)	0.357 (53)	0.435 (65)	0.588 (88)	was not examined				The original velocity was almost regained one hour after
25	0.667	0.667 (10)	0.667 (10)	0.083 (12)	0.111 (17)	0.149 (22)	0.196 (29)	0.232 (35)	was not examined				The original velocity was not regained even after one hour

TABLE VI RELATION BETWEEN REACTION BY RINGER'S SOLUTION AND DUST EXPELLING VELOCITY (WHEN HYDROCHLORIC ACID WAS USED AS ACIDIFIER)

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.00[illegible]	0.667	0.625 (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	Velocity was constant
0.01	0.667	0.625 (94)	0.625 (94)	0.667 (100)	0.667 (100)	0.667 (100)	0.714 (107)	0.667 (100)	Same as above
0.03	0.625	0.667 (107)	0.667 (107)	0.417 (67)	0.357 (57)	0.278 (44)	0.217 (35)	0.208 (33)	The velocity before application was regained 1 hour after
0.05	0.667	0.714 (107)	0.435 (65)	0.256 (38)	0.172 (26)	below 0.083 (<12) (*)	(-)	(-)	Motion was re-commenced 1 hour after but velocity was very slow
0.1	0.625	0.714	0.167 0.083 (27-13) (*)	below 0.083 (<12) (*)	(-)	(-)	(-)	(-)	Motion was not perceivable 1 hour after
0.3	0.625	0.714 (114)	(-)	(-)	(-)	(-)	(-)	(-)	Same as above

TABLE VII RELATION BETWEEN REACTION BY RINGER'S SOLUTION AND DUST EXPELLING VELOCITY (WHEN HYDROCHLORIC ACID WAS USED AS ACIDIFIER)

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.005	0.667	0.667 (100)	0.667 (100)	0.667 (100)	0.714 (107)	0.714 (107)	0.714 (107)	0.769 (115)	The velocity before the application was almost regained in approx. 15 minutes
0.01	0.625	0.625 (100)	0.625 (100)	0.625 (107)	0.625 (107)	0.714 (114)	0.714 (114)	0.667 (100)	At first the velocity was temporarily decreased but was restored in 15 min.
0.03	0.625	0.769 (121)	0.667 (107)	0.667 (107)	0.588 (94)	0.357 (57)	0.167 0.083 (27-13) (*)	(-)	The motion was restored in 30 min.
0.05	0.588	0.714 (121)	0.588 (100)	0.500 (85)	0.263 (45)	0.167 -0.083 (28-14) (*)	(-)	(-)	After 1 hour, motion was not recovered
0.1	0.667	2'(-)	(-)	(-)	(-)	(-)	(-)	(-)	Same as above

Incl A, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE VIII RELATION BETWEEN REACTION OF RINGER'S SOLUTION AND DUST EXPELLING VELOCITY (WHEN SODIUM BICARBONATE WAS USED TO MAKE THE SOLUTION BASIC)

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.1	0.625	0.625 (100)	0.625 (100)	0.625 (100)	0.667 (107)	0.667 (107)	0.714 (114)	0.833 (123)	The velocity before the application was restored in approx. 30 minutes
0.3	0.625	0.625 (100)	0.625 (100)	0.667 (107)	0.667 (104)	0.760 (123)	0.769 (123)	0.833 (133)	The velocity before the application was restored in approx. 30 minutes.
0.5	0.625	0.625 (100)	0.667 (107)	0.714 (114)	0.714 (114)	0.625 (100)	0.625 (100)	0.555 (89)	The velocity before the application was regained in approx. 45 minutes.
1.0	0.667	0.714 (107)	0.667 (100)	0.555 (83)	0.435 (65)	0.435 (52)	0.204 (31)	0.167-0.083 (25-21) (*)	The velocity before the application was regained 60 minutes after
3.0	0.555	0.588	0.400	0.232	0.167-0.083 (30-15) (*)	(-)	(-)	(-)	The motion was recommenced in 30 minutes
5.0	0.555	0.555 (100)	(-)	(-)	(-)	(-)	(-)	(-)	The motion was not recovered even 30 minutes after

TABLE XIV MAXIMUM AND MINIMUM VELOCITIES WITH VARYING ACIDITY AS WELL AS ALKALINITY OF SOLUTION

Chemicals	HCl	NaOH	$NaHCO_3$	HCl	NaOH	$NaHCO_3$
Concen-tration (%)	Maximum relative velocities, %			Minimum relative velocities, %		
0.005	100	115		94	100	
0.01	107	114		94	100	
0.03	107	123		33	0	
0.05	107	121		0	0	
0.1	114		123			100
0.3			133			100
0.5			114			89
1.0			107			12
3.0			106			0
5.0			100			0

TABLE X ADRENALIN CRYSTALS

Concentration of solution, %	Velocity before application, mm/sec	Time (min) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.1	0.714	0.714 (100)	0.667 (100)	0.714 (100)	0.714 (100)	0.667 (100)	0.714 (100)	0.714 (100)	The velocity was constant

TABLE XI ATROPINE SULPHATE

Concentration of solution, %	Velocity before application, mm/sec	Time (min) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.01	0.555	0.526 (100)	0.526 (100)	0.526 (94)	0.555 (89)	0.555 (94)	0.526 (89)	0.526 (89)	The velocity before application was regained 5 minutes after
0.03	0.625	0.625 (93)	0.625 (87)	0.588 (93)	0.555 (93)	0.588 (87)	0.555 (87)	0.555 (82)	Same as above
0.05	0.714	0.667 (87)	0.625 (87)	0.667 (93)	0.667 (93)	0.625 (87)	0.625 (87)	0.588 (82)	The velocity before application was regained in 10 minutes
0.1	0.714	0.625 (87)	0.625 (87)	0.625 (87)	0.625 (87)	0.625 (87)	0.288 (82)	0.555 (78)	Same as above
0.3	0.588	0.555 (94)	0.555 (94)	0.526 (89)	0.526 (89)	0.500 (85)	0.500 (85)	0.476 (81)	Same as above
0.5	0.667	0.500 (75)	0.500 (75)	0.500 (75)	0.500 (75)	0.500 (75)	0.476 (71)	0.454 (68)	Same as above

TABLE XII PILOCARPINE HYDROCHLORIDE

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.1	0.714	0.796 (108)	0.796 (108)	0.796 (108)	0.796 (108)	0.714 (108)	0.714 (108)	0.714 (108)	Velocity was constant
0.3	0.555	0.625 (112)	0.625 (112)	0.667 (120)	0.667 (120)	0.667 (120)	0.625 (112)	0.555 (100)	Same as above
0.5	0.526	0.667 (127)	0.714 (136)	0.667 (127)	0.667 (127)	0.588 (112)	0.555 (105)	0.500 (95)	The velocity before application was regained 5 minutes after

TABLE XIII PHYSOSTIGMINE SALICYLATE

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.1	0.667	0.667 (100)	0.625 (94)	0.625 (94)	0.667 (100)	0.667 (100)	0.667 (100)	0.625 (94)	The velocity before application was restored 6 minutes after
0.5	0.588	0.500	0.417	0.400	0.400	0.357	0.286	0.263	The velocity before application was not regained even 30 minutes after

TABLE XIV MORPHINE HYDROCHLORIDE

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.5	0.667	0.667 (100)	0.6[illegible] (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	Velocity was constant
1	0.625	0.625 (100)	0.625 (100)	0.667 (107)	0.667 (107)	0.588 (107)	0.555 (94)	0.500 (89)	The velocity before application was restored 15 minutes later
3	0.625	0.667 (107)	0.714 (114)	0.714 (114)	0.588 (94)	0.555 (89)	0.500 (89)	0.500 (80)	The velocity before application was restored 30 minutes later
5	0.526	0.270	0.270	0.250	0.172	0.167-0.083 (27-13) (*)	0.167-0.083 (27-13) (*)	below 0.083 (27-13) (*)	The velocity before application was not restored even 30 minutes later

TABLE XV COCAINE HYDROCHLORIDE

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	20'	45'	60'	
0,1	0.555	0.555 (100)	0.555 (100)	0.555 (100)	0.555 (100)	0.555 (100)	0.555 (100)	0.555 (100)	The velocity was constant
0.3	0.714	0.714 (100)	0.714 (100)	0.769 (108)	0.769 (108)	0.769 (108)	0.714 (100)	0.667 (93)	The velocity before application was restored approx. 5 minutes later
0.5	0.667	0.714 (107)	0.714 (107)	0.769 (115)	0.667 (100)	0.667 (100)	0.625 (94)	0.625 (94)	Same as above
1	0.555	0.625 (112)	0.625 (112)	0.625 (112)	0.555 (100)	0.526 (95)	0.454 (82)	0.400 (72)	The velocity before application was restored approx. 15 minutes later
3	0.667	0.769 (115)	0.667 (100)	0.555 (83)	0.500 (75)	0.263 (39)	0.167-0.083 (27-13) (*)	(-)	The original velocity was not regained even after 30 minutes later
5	0.667	0.769	0.588	0.454	0.256	below 0.083 (<13) (*)	(-)	(-)	The motion was not recommenced 30 minutes later
10	0.667	0.417 (79)	(-)	(-)	(-)	(-)	(-)	(-)	The motion was not recommenced even 30 minutes later

TABLE XVI A[illegible]

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.00001	0.625	0.625 (100)	0.625 (100)	0.625 (100)	0.625 (100)	0.625 (100)	0.625 (100)	0.625 (100)	Velocity was constant
0.00003	0.625		0.667 (107)	0.667 (107)	0.625 (100)	0.588 (94)	0.588 (94)	0.555 (89)	The original velocity was regained approx. 30 minutes later
0.00005	0.500		0.476 (95)	0.476 (95)	0.476 (95)	0.435 (87)	0.435 (87)	0.400 (80)	Same as above
0.0001	0.625		0.555 (89)	0.555 (89)	0.526 (84)	0.476 (76)	0.400 (64)	0.333 (53)	The original velocity was not regained even after 30 minutes later
0.0003	0.667		0.588 (88)	0.588 (88)	0.500 (75)	0.454 (68)	0.333 (50)	0.189 (28)	Same as above
0.0005	0.625		0.111 (18)	0.111 (18)	0.111 (18)	0.105 (17)	below 0.083 (<11) (*)	(-)	The motion was recommenced 30 minutes later
0.001	0.625		(-)	(-)	(-)	(-)	(-)	(-)	The motion was not recommenced even 30 minutes later

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Duration of expelling motion and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.0001	0.625	0.714 (114)	0.714 (114)	0.667 (107)	0.667 (107)	0.625 (100)	0.588 (94)	0.555 (89)	The original velocity was regained in approx. 30 minutes
0.0003	0.526	0.625 (119)	0.588 (112)	0.526 (100)	0.400 (76)	0.286 (54)	0.167–0.083 (27-13) (*)	below 0.083 (<13) (*)	The original velocity was not regained even 30 minutes later
0.0005	0.588	0.625	0.526	0.454	0.400	0.167–0.083 (28–14) (*)	(–)	(–)	The motion was restored 30 minutes later
0.001	0.769	(–)	(–)	(–)	(–)	(–)	(–)	(–)	The motion was not restored even 30 minutes later

TABLE XVIII ACETONE

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.3	0.667	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.667 (100)	0.625 (94)	0.667 (100)	Velocity was constant
0.5	0.833	0.833 (100)	0.833 (100)	0.833 (100)	0.833 (100)	0.833 (100)	0.909 (109)	0.909 (109)	The original velocity was regained in approx. 10 minutes
1	0.667	0.714 (114)	0.667 (100)	0.588 (88)	0.526 (79)	0.476 (71)	0.435 (65)	0.345 (52)	The original velocity was regained in approx. 30 minutes
3	0.625	0.714 (114)	0.555 (89)	0.417 (67)	0.333 (53)	0.278 (44)	0.244 (39)	0.196 (31)	The original velocity was not restored even 30 minutes later
5	0.714	0.526 (74)	0.345 (52)	0.322 (48)	0.250 (37)	0.137 (20)	below 0.083 (<11) (*)	(-)	The motion was restored approx. 30 minutes later
10	0.555	(-)	(-)	(-)	(-)	(-)	(-)	(-)	The motion was not recommenced even 30 minutes later

Incl 7. Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE XIX CREOSOTE

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
0.01	0.625	0.714 (114)	0.714 (114)	0.769 (123)	0.714 (114)	0.714 (114)	0.667 (107)	0.667 (107)	The original velocity was regained approx. 15 minutes later
0.03	0.526	0.526 (119)	0.526 (119)	0.667 (127)	0.667 (127)	0.625 (119)	0.588 (112)	0.588 (112)	Same as above
0.05	0.588	0.714 (121)	0.769 (131)	0.769 (131)	0.769 (131)	0.769 (131)	0.714 (121)	0.667 (131)	Same as above
0.1	0.704	0.625 (81)	0.588 (82)	0.500 (70)	0.500 (70)	0.476 (67)	0.454 (63)	0.400 (63)	The original velocity was regained approx. 30 minutes later
0.3	0.500	0.238	0.232	0.167	0.167-0.083 (33-16) (-)	(-)	(-)	(-)	The motion was recommenced 30 minutes later
0.5	0.625	(-)	(-)	(-)	(-)	(-)	(-)	(-)	The motion was not recommenced even 30 minutes later

Incl 7, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE XX CAMPHOR

Concentration of solution, %	Velocity before application, mm/sec.	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
Saturated	0.714	0.357 (50)	0.263 (37)	0.141 (20)	0.090 (13)	(-)	(-)	(-)	The motion was not recommenced even 30 minutes later
1/2 saturated	0.625	0.555 (89)	0.476 (76)	0.385 (62)	0.322 (51)	0.278 (44)	0.232 (37)	0.178 (28)	The original velocity was not regained even 30 minutes later
1/3 saturated	0.625	0.555 (89)	0.555 (89)	0.476 (76)	0.476 (76)	0.435 (70)	0.417 (67)	0.417 (67)	The original velocity was regained 30 minutes after
1/5 saturated	0.769	0.667 (87)	0.667 (87)	0.714 (93)	0.714 (93)	0.714 (93)	0.769 (100)	0.769 (100)	The original velocity was regained 30 minutes after
1/10 saturated	0.667	0.714 (107)	0.714 (107)	0.714 (107)	0.714 (107)	0.714 (107)	0.667 (100)	0.667 (100)	Same as above
10% camphorated oil	0.526	0.294 (56)	0.294 (56)	0.286 (54)	0.232 (44)	0.217 (41)	0.213 (40)	0.208 (39)	The original velocity was not regained even 30 minutes later

TABLE XX CONT'D

Camphorated steam current	0.588	0.588 (100)	0.588 (100)	0.588 (100)	0.588 (100)	0.588 (100)	0.625 (106)	0.625 (106)	The original velocity was regained in approx. 5 minutes
Camphorated steam	0.625	0.625 (100)	0.588 (94)	0.286 (46)	0.250 (40)	0.250 (40)	0.244 (39)	0.147 (25)	The original velocity was regained approx. 30 minutes later

TABLE XXI MENTHOL

Concentration of solution, %	Velocity before application, mm/sec	Time (min.) which elapsed and dust expelling velocity (mm/sec)							Restoration of expelling action and remarks
		3'	5'	10'	15'	30'	45'	60'	
Saturated	0.667	0.625 (94)	0.625 (94)	0.588 (88)	0.555 (83)	0.555 (83)	0.476 (71)	0.476 (71)	The original velocity was regained approx. 30 minutes later
1/2 saturated	0.588	0.588 (100)	0.625 (106)	0.555 (94)	0.555 (94)	0.526 (89)	0.476 (81)	0.435 (74)	Same as above
1/5 saturated	0.588	0.588 (100)	0.588 (100)	0.625 (106)	0.555 (94)	0.555 (94)	0.500 (85)	0.500 (85)	The original velocity was regained in approx. 10 minutes
1/10 saturated	0.625	0.625 (100)	0.625 (100)	0.625 (100)	0.625 (100)	0.667 (107)	0.667 (107)	0.667 (107)	The original velocity was regained in approx. 10 min.

TABLE XXI CONT'D

Menthol steam current	0.625	0.667 (107)	0.667 (107)	0.769 (123)	0.769 (123)	0.714 (114)	0.667 (107)	0.667 (107)	The original velocity was regained in approx. 10 minutes
Menthol steam	0.588	0.435 (74)	0.345 (59)	0.312 (53)	0.167-0.083 (28-14) (*)	below 0.083 (14) (*)	(-)	(-)	The motion was recommenced in approx. 30 min.

COMPARATIVE STUDY OF DUST EXPELLING
VELOCITY IN TRACHEA OF ANIMALS OF VARIOUS AGES

By

Dr. Masanobu SAITO, Department of Hygiene,
Faculty of Medicine, Kyoto University, Kyoto.

ABSTRACT

(Published in National Hygiene (Japan), 9, 407-414 (1934))

Introduction:

Dust expelling velocity experiments in the past were always performed by using adult animals and not infant animals. The author has carried out the experiment with extracted trachea of younger animals as well as those of adult animals to ascertain if the degree of matureness has any influence upon the dust expelling velocity.

Test Materials and Experimental Procedures:

Fresh trachea extracted from rabbits and dogs were mounted on cork plates (10 cm long, 5 cm wide, and 1.5 cm thick) with pins and suspended in a glass cylinder thermostatically maintained at 39°C. The dust particles and the experimental technics used in the experiment were the same as explained in the previous report (SAITO, National Hygiene (Japan), 9, 395-406 (1934))

Experimental Results:

Experimental results are tabulated in Tables I, II, III, and IV.

TABLE I DUST EXPELLING VELOCITY OF EXTRACTED TRACHEA, RABBITS AND DOGS

Species of Animal	Age, Months	Time Required for Dust Particles to be Transported 1 cm Distance, sec. Extracted Trachea Test Piece Number I	II	III	IV	V	Mean Value
Rabbits	1	110	120	130	170	120	130
	2	60	80	65	91	80	73
	3	48	49	55	50	51	51
	4	30	37	34	40	32	37
	5	25	26	27	26	30	24
	6	20	23	23	25	30	24
Dogs	Young	60	57	80	75	45	63
	Adult	21	22	23	24	19	22

TABLE II RELATIONSHIP BETWEEN DUST EXPELLING VELOCITY AND ELAPSE OF TIME, RABBITS

Test Piece of Extracted Trachea, Number of Months after Birth	Dust Expelling Velocity Expressed in Time (sec) to Transport Dust Particle 1 cm Distance after Indicated Elapse of Time						
	5 min	10 min.	30 min.	1 hour	2 hours	3 hours	6 hours
1	$\underline{*}$	$\underline{*}$	$\underline{*}$	-	-	-	-
2	*	*	$\underline{*}$	-	-	-	-
3	50	55	*	$\underline{*}$	-	-	-
4	32	30	32	*	$\underline{*}$	-	-
5	25	25	26	*	$\underline{*}$	-	-
6	23	24	24	*	$\underline{*}$	$\underline{*}$	-

NOTES: * indicates 1 - 2 minutes.
$\underline{*}$ indicates over 2 minutes.
- indicates cessation of movement.

TABLE III RELATIONSHIP BETWEEN DUST EXPELLING VELOCITY AND THE SIZE OF THE TRACHEA

Approximate Diameter of Trachea at its glottis-erweiterer, cm	Approximate Distance from glottis erweiterer to Bronchial Junction, cm	Dust Expelling Velocity Expressed in Time (sec) to transport Dust Particles 1 cm Distance for Extracted Trachea of Rabbits by Samples				
		1	2	3	4	5
0.4-0.5	2-3	110	120	130	170	120
0.5-0.6	3-4	60	90	65	91	80
0.6-0.7	4-5	48	49	55	51	50
0.6-0.8	5-6	30	37	34	40	32
0.6-0.9	6-7	25	26	27	26	30
0.7-1.0	7-9	20	23	23	30	25

[illegible] Report TIL, GHQ, FEC, APO 500, Subject: "Locus of Impaction of Particulates", dated 15 Dec 48

TABLE IV RELATIONSHIP BETWEEN DUST EXPELLING VELOCITY AND SIZE OF DUST PARTICLES IN RABBITS.

Size of Dust Particles		Dust Expelling Velocity expressed in Time (sec) to Transport Dust Particles 1 cm Distance for Extracted Trachea of Rabbits by Age					
Sieve Number	Maximum and Minimum Diameter, mm	1 month	2 months	3 months	4 months	5 months	6 months
1	less than 0.043	$\underline{*}$	*	50	30	25	20
2	0.043-0.053	$\underline{*}$	*	49	34	26	24
3	0.053-0.061	$\underline{*}$	*	50	34	27	24
4	0.061-0.074	$\underline{*}$	*	50	33	25	27
5	0.074-0.088	$\underline{*}$	*	51	31	24	24
6	0.088-0.108	$\underline{*}$	$\underline{*}$	*	48	25	25
7	0.108-0.147	$\underline{*}$	$\underline{*}$	$\underline{*}$	50	30	30
8	0.147-0.208	-	-	-	55	45	40
9	0.208-0.495	-	-	-	*	*	*
10	0.495-0.991	-	-	-	-	-	-

NOTES: * indicates 1 - 2 minutes.
$\underline{*}$ indicates over 2 minutes.
\- indicates cessation of movement.

Conclusions:

The dust expelling velocity in infant animals are very slow in comparison with adult animals as shown in Table I.

The degree of retardation in the dust expelling velocity due to the elapsing of time varies upon the matureness of the animals; i.e. the younger animals have shorter period during which the extracted trachea is able to expell the dust particles, as shown in Table II.

It was revealed, as shown in Table III, that among same species of animals of equal matureness, the dust expelling velocity became slower as the size of the trachea became smaller.

Through the author's experiment in which adult rabbits as well as infant rabbits were made to inhale charcoal dust particles of various sizes (see Table IV), it was shown that in the case of the infant rabbits,

only a very small amount of dust deposited in the trachea and comparatively large amount of dust particles are allowed to enter the trachea in the case of the adult animals. These experimental data indicates that dust particles which are too large to be expelled will never enter the trachea in the normal inhalation.

PATHOLOGICAL CHANGES OF THE MUCOUS MEMBRANE OF TRACHEA BY CONTINUOUS INHALATION OF VARIOUS POISONOUS GASES AND THEIR RELATIONSHIP WITH FOREIGN BODY EXPULSION ACTION

By

Kazuo TAKEUCHI and Minoru YANAGIBASHI

Hygienic Laboratory, Faculty of Medicine, Kyoto University

ABSTRACT

(Published in National Hygiene (Japan), II, 1447-1462 (1935))

1. INTRODUCTION

The development of chemical industries has become a hazardous problem since various ailments are being caused by poisonous gases which are generated in various types of factories in the course of their operation. As a result, some valuable studies have been conducted by our predecessors on the poisoning action of poisonous inorganic gases, such as sulphur dioxide, hydrogen sulfide, and carbon disulfide, which are widely used in industries closely related with our life. Few reports are yet available except for those by NAGATANI, SAITO and TAKEUCHI of this laboratory and LOMMEL on the expulsion action of foreign bodies from the trachea.

SAITO (National Hygiene (Japan), 10, 473 (1934)) has conducted research with regard to the checking action of poisonous gases by studying the dust expulsion action of extracted trachea. The purpose was to discover whether or not a habituation process develops on the part of the trachea or not. The results revealed that the trachea developed its tolerance comparatively well against sulphur dioxide, but no such habituation against hydrogen sulfide and carbon disulfide. A patho-histological examination of the mucous membranes of the trachea and the observation of the speed of foreign body expulsion action were carried out in order to obtain some reliable data on the development of its tolerance. When rabbits inhaled vapors of sulfurous acid, nitrous acid, hydrogen suldide and carbon disulfide, retardation or suspension of the foreign body expulsion action were observed and the development of tolerance with the increasing concentration and interval of application were noted. The order of decreasing reaction were as follows: sulfur dioxide, nitrous acid, hydrogen sulfide, hydrochloric acid, and carbon disulfide.

According to TERAMOTO (J. Aichi Medical Association (Japan) 4, 472), guinea pigs showed pathological changes such as desquamation of the epithelial cells, various types of involutional degenerations, partial extinguishment of the epithelium, etc, on the mucous membranes in the upper part of their trachea and round cell infiltration, dilation and inflammation of blood vessels, death of some gland cells, formation of vesicles, etc. in the sub-mucous membrane tissues when carbon disulfide and sulfur dioxide were inhaled.

Incl 9. Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

NAGATIANI (National Hygiene (Japan), 7, No. 9) sprayed sulfurous acid, hydrogen sulfide and hydrochloric acid vapors on the extracted windpipe of oxes and examined its action. The expulsory function of the windpipe ceased in 1-2 minutes even with dilute concentration of the acids.

2. MATERIAL AND METHOD USED IN THE EXPERIMENT

A certain number of rabbits were put into several chambers, each containing different concentrations of sulfur dioxide, hydrogen sulfide, or carbon disulfide, for one hour each day for a period of a month. Then, they were killed and the foreign body expulsion action of the trachea and its histological changes were investigated by extracting their windpipes.

a. Test Animals: Two healthy rabbits, each about 2 kg weight, were used for each gas. The rabbits were fed fresh bean-curd refuse. If evidences of ailments appeared, the rabbits were taken out of the experiment.

b. Apparatus Used in the Experiment: Oblong boxes, 41 to 53 liter capacity, equiped with a glass observation window on one side and an airtight door with gum packing in the ceiling were used. The experiment was commenced after chemicals had completely volatized and permeated the boxes which was placed in a thermostatic chamber maintained at 18-20°C.

c. Chemicals Used in the Experiment: Saturated aqueous solutions of sulfur dioxide and hydrogen sulfide, freshly obtained form the local factory, were used. Carbon disulfide was Merck's product.

d. Concentration of the Vapor: At first, vapors of low concentration were given to the test animals for a certain number of hours a day and continued for several days. When no pronounced effects were observed, the concentration of the vapor was gradually increased. Details are tabulated in Table I.

e. Method of Measuring the Foreign Body Expulsion Action: When the test animal had inhaled the gases for one hour per day for 30 days, their windpipes were extracted as promptly as possible and put into a thermostatic apparatus maintained at 39°C by employing the same experimental apparatus and method as NAGATANI's. The foreign body expulsion rate was measured by using grains of carbon powder ranging in size from 0.074 to 0.088 mm.

f. Method of Preparing Specimens: The windpipes were placed in ortho solution from one to two days, washed with water for about the same period and dehydrated. Then, they were cut into continuous sections according to the Colloidin Wrapping Method and the specimen were stained with haematoxylin-eosin dye for microscopic examinations.

TABLE I EFFECT OF POISONOUS GASES.

Number of Days	Sulfurous Acid Amount Used, cc	Sulfurous Acid Gas Concentration mg/L	Sulfurous Acid Weight of Animal kg	Hydrogen Sulfide Amount Used, cc	Hydrogen Sulfide Gas Concentration mg/L	Hydrogen Sulfide Weight of Animal kg	Carbon Disulfide Amount Used, cc	Carbon Disulfide Gas Concentration mg/L	Carbon Disulfide Weight of Animal kg
1	1	2.8	#1 2.1 #2 2.05	30.0	2.9	#3 2.0 #4 2.1	0.2	417	#5 2.1 #6 2.25
2	"	"	"	"	"	"	"	"	"
3	"	"	"	"	"	"	"	"	"
4	"	"	"	"	"	"	"	"	"
5	"	"	"	"	"	"	"	"	"
6	"	"	"	"	"	"	"	"	"
7	"	"	#1 2.0 #2 1.9	"	"	#3 2.0 #4 2.0	"	"	#5 2.0 #6 2.1
8	"	"	"	"	"	"	"	"	"
9	"	"	"	"	"	"	"	"	"
10	"	"	"	"	"	"	"	"	"
11	1.5	4.2	"	40.0	3.8	"	0.3	7.1	"
12	"	"	"	"	"	"	"	"	"
13	"	"	"	"	"	"	"	"	"
14	"	"	"	"	"	"	"	"	"
15	"	"	"	"	"	"	"	"	"
16	2.0	5.6	#1 1.8 #2 1.75	50.0	4.6	#3 1.8 #4 1.8	0.4	9.5	#5 1.9 #6 2.0
17	"	"	"	"	"	"	"	"	"
18	"	"	"	40.0	3.8	"	"	"	"
19	"	"	"	30.0	2.9	"	"	"	"
20	"	"	"	40.0	3.8	"	0.3	7.1	"
21	"	"	"	"	"	"	0.4	9.5	"
22	"	"	"	"	"	"	"	"	"
23	"	"	"	"	"	"	"	"	"
24	"	"	#1 1.5 #2 1.5	"	"	#3 1.8 #4 1.8	"	"	#5 1.9 #6 2.0
25	"	"	"	"	"	"	"	"	"
26	"	"	* "	"	"	"	"	"	"
27	"	"	"	"	"	"	"	"	"
28	"	"	"	"	"	"	"	"	"
29	"	"	"	"	"	#3 1.75 #4 1.8	"	"	#5 1.9 #6 1.95
30	"	"	"	"	"	"	"	"	"

NOTE: * Rabbit #1 contracted diarrhoea.

Incl 9. Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE II FOREIGN BODY EXPULSION SPEED AND SPEED AND STATE OF RECOVERY

Type of Gas	Animal Number	Expulsion Speed in Healthy Rabbit	Time Elapsed (Min.) after the Extraction of Windpipe and Expulsion Speed 0	5	10	15	30	45	60	120	Rate of Recovering Expulsion Function.
Sulfurous acid	1	Av. Expulsion speed: 0.416 mm/sec	±	±	±	±	±	+	+	+	Average Recovery after 3 hr
	2		o	±	±	±	±	±	+	+	40-20%
Hydrogen sulfide	3	"	o	o	o	o	o	±	±	±	Less than 20%
	4	"	o	o	o	o	o	o	±	±	"
Carbon disulfide	5	"	o	o	o	o	o	±	±	+	40-20%
	6	"	o	o	o	o	o	o	±	+	"

NOTE: + 0.107-0.083 mm/sec (40-20%)
± Less than 0.083 mm/sec (Less than 20%)
o Disappearance of function

Incl.9. Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

3. RESULTS

a. Clinical Observations:

Sulfur dioxide: Soon after the beginning of the experiment, Animals Numbers 1 and 2 closed their eyes, shed tears and appeared to be in panic, unrest, rubbing their faces, especially around their mouths with their paws. When 10-20 minutes had passed, they squatted down in a corner of the boxes. After 30-40 minutes their breathing rate began to increase, and at times, they had difficulties. When the rabbits were returned to their basket, they sat quietly in a corner for a short period and regainde their normal conditions in about 20 to 30 minutes. Toward the end of the experiment, the rabbits showed marked decrease in weight, see Table I.

Hydrogen sulfide: Animals Numbers 3 and 4 behaved very similar to those in the sulfur dioxide experiment for the first few minutes. After 10-20 minutes, the animals squatted in a corner of the box and commenced profuse secretions from their mouths and nostrils. The rate of breathing began to increase in the early stages of the experiment, but no difficulties were noted. When the concentration of the gas was increased from 3.8 to 4.6 mg/L. on the sixteenth day, both rabbits closed their eyes and began shedding tears upon beginning of the experiment. Soon thereafter, panic and pain appeared to have seized them; profuse secretions began to come from their mouths and nostrils accompanied by increased rate of breathing. After 30-40 minutes of pain, they suddenly began to toss about for a short time and collapsed. Their rate of breathing was markedly increased and developed into a serious condition so that the experiment was reduced to 54 minutes instead of an hour. Rabbits required a longer period in which to revert to normal conditions. No noticeable decrease was observed in their appetite throughout the course of the experiment.

Carbon disulfide: Five to seven minutes after the beginning of the experiment, animals #5 and #6 closed their eyes and commenced shedding tears. Their breathing became difficult and showed signs of panic. After 20-30 minutes the rate of breathing increased from 7.1 to 9.5 mg/L. on the sixteenth day, they showed no serious symptoms for two or three days. Four days later, they suddenly showed marked difficulty in breathing after 30-40 minutes by tossing around in a very weak manner. Therefore, the experiment was terminated after 50 minutes duration instead of an hour. The animals regain health within a reasonable time. For the initial 4-6 days of the experiment, the animals showed poor appetite, but they returned to normal thereafter.

b. Foreign Body Expulsion Speed of Windpipe: The results of the foreign body expulsion speed and the state of recovery after inhaling poisonous gases for 1 hour a day for a period of 30 days are tabulated in Table II.

c. Anatomical Observations:

Sulfur dioxide: Animal numbers 1 and 2 showed a remarkable symptoms of irritation and inflammation on the mucous membranes of the windpipes. The lungs were slightly dark red, while the livers and the spleens showed no changes.

Hydrogen sulfide: Animal Numbers 3 and 4 showed pronounced symptoms of irritation on the mucous membranes of their trachea. In the lower and central lobe of animal number 3's left lung were found images of catarrhalic pneumonia. No pathological changes such as the congestion or swelling of the spleens and livers were detected.

Carbon disulfide: Animal Numbers 5 and 6 showed a pronounced bleeding and secretion in the mucous membranes of their windpipes. Both lungs of the animals were dark red and showed symptoms of hemorrahagic pneumonia. No abnormal changes were observed in their livers and spleens.

d. Histological and Pathological Observations: The histological and pathological observations for each test animal were as follows:

Animal No. 1: The ciliated columnar epitheliums of the mucous membranes of the trachea were found somewhat shortened with the surface layer cells being dearranged to a great extent or desquamated. Some vesicles and encysted tumours were also found in the epithelial layers. Marked proliferations of the connective tissues accompanied by pronounced round cell infiltrations were observed in the tissues of the epithelial layers. The blood vessels showed a slight dilation and congestion, while the gland cells were found obscured and stained with pus at some spots. No changes were otherwise detected in the cartilaginous tissues and other parts.

Animal No. 2: The epitheliums of the mucous membranes of the trachea showed a pronounced degeneration, desquamation and flattening of the surface layer cells. Few vesicles were found in the layer. Comparatively dense rounded celled infiltrations were observed in the layer, while the blood vessels showed only a slight dilation and congestion.

Animal No.3: The surface layer cells of the cilliated columnar epithelium of the mucous membrane of the trachea were considerably desquamated so that the surface layer was deformed into a flat epithelium at various spots like scattered islands with some of them occupying a large area. Many vesicles and encysted tumors containing a water-like fluid were formed in the epithelial layer making it tough and coarse. The connective tissues showed a marked increase in the number of proliferations accompanied by a pronounced round celled infiltrations. Dilation and inflammation of the blood vessels was comparatively slight, though the walls were swollen to some degree. The gland tissues showed a contractive degeneration and some of the gland cells were transformed into vesicles or completely collapsed. No changes were observed in the cartilaginous tissues and other parts.

Animal No. 4: All the symptoms were more of less similar to those with Animal No. 3, except that the gland cells were infected with pus.

Animal No. 5: The cilitated columnar epitheliums of the mucous membrane of the trachea were swollen and infected. The locally degenerated, desquamated or flattened. Symptoms of edema were observed in the connective tissues of the epithelium layer. Dilation and inflammation of the blood vessels were observed and they were accompanied by a slight bleeding at some spots. Roundcell infiltration was found in the tissues around the blood infected with pus, while others were found either forming vesicles or having damaged nuclei. No pathological changes were observed in the cartilaginous tissues.

Animal No. 6: The pathological changes were somewhat mitigated version of those observed in Animal No. 5.

The pathological changes commonly observed in the mucous membrane of the three cases are as follows: (1) the degeneration, desquamation and flattening of the surface cells, and the formation of vesicles and cerebral vesicles in the columnar epitheliums. (2) roundcell infiltration, infection of the gland cells with pus, and the formation and collapse of the vesicles in the layer proper.

The flattening of the cilitated columnar epithelium membranes are considered to be mainly due to chemical stimulations by poisonous gases and a catarrhal, or inflammatory irritation caused by the said stimulation, whose combined effects degenerate and desquamate the epithelial cells.

The formation of vesicles and cerebral vesicles are also due to the chemical stimulations of poisonous gases. It appears that when the epithelial cells are degenerated and collapsed by inhaled gases, the affected spots are invaded by many migratory cells. Coupled with the eruption, these cells eventually form a mass which leads to the formation of cerebral vesicles by oppressing the surrounding cells.

4. DISCUSSIONS

According to SAITO, as well as FLURY and ZERNIK, the foreign body expulsion action of the trachea acquires a tolerance to a certain extent against sulfurous acid, but no such habituation process takes place in the case of inhaling hydrogen sulfide. On the contrary, this experiment showed an increase in sensitivity and the reaction was further strengthened when carbon disulfide was used. The histological examinations revealed that sulfur dioxide affected only the surface of the mucous membranes, scarcely extending its influence into the deeper layers, while hydrogen sulfide and carbon disulfide affected not only the surface but also the deeper layers of the membrane by causing degenerative contraction.

It is considered that sulfurous acid confines its influence only to within the surface layer where oxidation to sulfuric acid which irritates the layer tissues, takes place. Carbon disulfide and hydrogen sulfide, however, do not react in the same manner. They do not undergo any chemical changes on the surface layer, but they penetrate deep into the tissue. At the same time they adhere to or dissolve the fat element in the mucous membrane tissues. Their effects are cumulative and gradually causes contractive degeneration of the tracheal tissues.

EXPERIMENTAL CONTRIBUTION TO THE STUDY OF PULMONARY ANTHRACOSIS IN RABBITS

By

Kaneyoshi AKAZAKI and Fujio NITTONO

Department of Pathology, Niigata Medical College

ABSTRACT

(Published in the Transaction of the Society of Pathology, Japan, 31: 326-333 (1941).

1. Introduction:

By examinations of the human bodies by autopsy and by the experimental researches on pneumoconiosis with animals, it has been made clear to some extent that the morphological changes of the lungs caused by various kinds of pneumoconiosis differs according to the type of dust inhaled.

The fibrous changes of the lungs and their lymphatic nodules which are often witnessed in anthracosis are attributable to the existence of the quartz dusts. This is confirmed by the experimental researches of ARNOLD, GROSS, and BORCHARD, who agree among themselves that the soot dust eventually causes no proliferation of the connective tissues of the lungs. Such are the opinions of the predecessors, but in the authors opinion their experimental results are not conclusive because the experiments were conducted long enough to allow an adequate comparison with the human pneumoconiosis nor did they make a thorough morphological study of the subject from the standpoint of the present advanced histology. Hence, further detailed research into the subject is necessary.

Furthermore, there are still a large number of unsolved problems concerning pneumoconiosis and others on how dusts penetrate from the alveolar cavities into the lung interstices, and how the soots once deposited in the interstices are transported to other parts.

By commencing with these ideas, the authors resumed the research project on anthracosis previously conducted and published in ZIEGLER's treatise, on a long term experiment extending over a 2 year period by using rabbits.

The authors were aware that the chemical composition of each soot dust, such as oil, charcoal, and several other coal soots, varied from one another according to the nature of the burnt materials.

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

2. Method of Experiment:

The test rabbits were placed for a period of 30 minutes every day in dust filled cages specially designed for the purpose of inhaling finely pulverized soots. The soots used for this experiment were obtained by burning a mixed fuel of 3 parts xylol and 1 part turpentine oil.

3. Results of the Experiment:

a. The Records of the Experiment, Macroscopic Examination of the Lungs and the Lymphatic Nodules of the Pulmonary Hilus:

The duration of the experiment, weight of the animals (beginning and termination), and the macroscopical findings of both the lungs and the lymphatic nodules of the pulmonary hilus of all the test animals are summarized and tabulated in Table I.

Though the dusts were stirred vigorously and persistently every day, they did not seem to affect the growth of the test animals, but kept increasing in weight. Hence one may infer that the inhalation of soots does not exert any pronounced effects upon the growth of the rabbits. However, as reported by earlier researchers, many test animals easily died because of bronchial pneumonia complications. On the other hand, authors also noted that certain rabbits died without leaving any evidences of pneumonia complications. It is also evident from the accompanying table that the degree of soot deposition is not always co-extensive with the length of the experiment, although the whole group of rabbits were treated entirely under the identical conditions of dust concentration. These facts may possibly be accounted for by the individual differences of disposition among the animals.

Further, it must be noted that the depostion of soots in the experimental research appears first and most pronounced in the peripheral parts of each lung lobes, especially in the surroundings of the pleural ribs and on the pleural diaphragms (Animal numbers 87, 88, 8, 81 and 6). Later, however, both upper lobes, especially both apexial areas of the lungs, became more likely places for the development of the experimental anthracosis (Animal Numbers 19 and 7), a fact which was not found in the case of human anthracosis (NITTONO). Such differences are apparently attributed to the differences in the intensity of the dust concentration between the human breathing and the test animal experiment.

TABLE I.

[illegible]ATION OF LUNGS AND LYMPHATIC NODULES OF PULMONARY HILUS

Rabbit No.	Duration of Experiment, days	Physical Weight		Nature of Termination	Macroscopic Observation	
		Commencement, g	Termination, g		Lungs	Lymphatic nodules of pulmonary hilus
86	16	860		died (b.p.)	Left lung: Extensive confluent bronchial pneumonia, milliary sized depositions (++); Right lung: similar soot deposition (++); Engorgement (++)	Undetectable
87	123	1950	2200	killed	Flecky soot deposition at the point where pleural ribes overlapped with pleural diaphragms in lower lung lobes (+)	Diffusive fine soot deposition (+)
88	123	1000	1300	killed	Point formed or flecky soot deposition at the point where pleural ribes overlapped with pleural diaphragm in lower lung lobes (++)	Same as Animal No. 87
85	155	1970	2350	died	Engoregement (++); Soot deposition (+)	Undetectable
89	224	2200	2540	died	Engorgement (+++); Flecky or threadlike soot deposition at the point where pleural ribs overlapped with pleural diaphragm (++)	Diffusive fine soot deposition (+)
83	246	2000	2760	killed	Engorgement (+)	Soot deposition (+)

TABLE I CONT'D

[illegible]	305	2610	3730	killed	Point formed soot deposition at the point where pleural ribs overlapped with pleural diaphragm (+)	Undetectable
10	330	2280	2900	died (b.p.)	Left lung: Confluent bronchial pneumonia. Right lung: Engorgement (+++); soot deposition (+)	Diffusive fine soot deposition
19	366	2220	3050	killed	Distinct flecky soot deposition especially at both apexes and at the point where pleural ribs overlapped with pleural diaphragm (+++)	Almost diffusive fine soot deposition (++)
20	366	2450	3100	killed	Soot deposition resembled Animal No. 19 (++) to (+++)	Same as Animal No. 19
9	457	2220	3290	killed	Engorgement (++); Soot deposition at the point where pleural ribs overlapped with pleural diaphragm (+)	Same as Animal No. 10
7	737	2220	3580	died	Partly diffusive or partly flecky soot deposition on both upper lung lobes (++++); Soot deposition at the point where pleural ribs overlapped with pleural diaphragm (+++)	Almost diffusive fine soot deposition (++)

NOTES: b.p. abbreviation for bronchial pneumonia; (+), (++), (+++) and (++++) represents relative intensities.

b. Histological Examinations:

(1) Examination of the Lungs:

Bronchi

None of the soot dusts inhaled seemed to have been received by the bronchial epitheliums or resorbed through the intercellular lymphatic crevices of the bronchial wall. However, appreciable amount of soots which were either ingested by the dust cells or mixed in a free state in the mucous mass were often found in the bronchial cavities. Apparently these soot dusts first penetrated into the alveolar cavities, then received by the alveolar epithelims, and finally discharged.

Alveoli

As repeatedly mentioned in our previous reports, the soots found in the alveolar cavities existed either in a free state or ingested by the epitheliums which were either stuck fast to the alveolar wall or freed therefrom into the alveolar cavities. In this case the free dust cells were always found to have ingested more soots than the cells stuck to the walls. Such scattered soot ingested cells (soot cells) were found to be disseminated all over the lungs in all cases examined regardless of the length of the experiment. What is more noteworthy, however, was the collection of the intracellular and extracellular soot dusts in some of the adjacent alveoli. This fact was noted and reported earlier by many researchers, but no attempts have been made by them to explore the exact histological image and the nature of this remarkable soot deposition.

For these reasons, the authors set out to make a thorough study of the facts found concerning the soot deposition. In the case of the 16 day inhalation test (Animal No. 86) the alveoli were found full of soots. Presumably part of such soot dusts made a mass deposition among the cells, but the authors were yet unable to determine how much of it remained in the cells themselves. The neutrophile leucocytes were also found among the intra-alveolar soot depositions. The alveolar-septa of the alveolar walls were always found atelectatically crumbled, though the interstitial connective tissues were not yet proliferated. In the inner structure of such alveoli, the alveolar epitheliums were found appreci-

ably proliferated, even merged with one another to form a continuous epithelial arrangement. It may also be pointed out that in the case under discussion (Animal No. 86) the bronchial pneumonia colonies that developed as complications showed pronounced glandular arrangement of pseudometaplastic alveolar epitheliums. However, the proliferated epitheliums showed no soot depositions.

These crumble alveolar epitheliums filled with soot dusts, as reported by GROSS and BROCHARD, were deposited in the immediate sub-pleural, peri-bronchial or peri-vascular sections, that is, in those parts which are more or less likely to be affected by the respiratory movement, but they were seen to be gradually removed from these tissue parts as was proven experimentally by the examination of the slide sections. Such characteristic deposition of soot in some of the adjacent alveoli was observed in all cases examined except a few cases (Animal Numbers 83 and 81).

The longer the experiment was continued, the greater became the atrophy of the soot choked alveoli and more increased became the thickening of the alveolar walls (Animal Numbers 19 and 7). The enormous thickening of the walls of such alveoli was brought about chiefly by the cellular hyperplasia. Besides the alveolar epitheliums, the proliferation of the spindle cells of the histiocytes and connective tissues by the infiltration of neutrophile leucocytes was observed.

Although the epithelial proliferation was very distinct in the thickened parts of the wall, the epithelial cells seldom ingested soot dusts. Nowhere in those soot choked alveoli was any sign of organization processes. A fairly appreciable amount of soots was found imbedded in a free state in the tissue crevices or occasionally ingested by the reticular or connective tissue cells.

Interstices:

Nothing conclusive can yet be said concerning the conditions under which the soot dusts passed from the alveolar cavities into the interstices. But from the fact that the soot dusts were found deposited in the interstices of the alveolar wall and also of the peri-bronchial or peri-vascular tissues, mostly in a free state in the tissue crevices or lymphatic vessels, or else ingested sparsely by the histiocytes,

with proliferation [illegible] was [illegible] to [illegible] epithelium [illegible]. As long [illegible] had been [illegible] (Animal [illegible] Fig. [illegible]) [illegible] proliferation [illegible] developed [illegible] around [illegible] alveolar epithelium. [illegible] the proliferation [illegible] [illegible].

[illegible] as reported by [illegible] and [illegible] (Animal [illegible]) [illegible] bronchi [illegible], that is, in those [illegible] to be affected by the [illegible], but [illegible] the [illegible] removed [illegible] by the [illegible] of the [illegible] of [illegible] in [illegible] (Animal Numbers [illegible] and 81).

The longer the [illegible] was continued, the [illegible] the [illegible] and the [illegible] of the [illegible] cells [illegible] 1 and 7). The [illegible] of the [illegible] was [illegible], the proliferation of the [illegible] and [illegible] the [illegible] of [illegible] was [illegible].

Although the [illegible] proliferation was [illegible] of the [illegible], the [illegible]. [illegible] any sign of [illegible]. A [illegible] amount of [illegible] was found [illegible] in [illegible] of [illegible] (Animal [illegible]).

[illegible]

[illegible] one [illegible] from the [illegible]. But [illegible] in the [illegible] and [illegible] [illegible].

[illegible] subject: "[illegible]"

fibroblasts or connective tissue cells, it can be inferred that the soot dusts should be found in a free state along the route of the lymphatic circulation. The soot dust in the free state was found in the largest amount in the alveolar wall of the soot packed alveolar groups and in a lesser amount, somewhat sparsely, imbedded in the peri-bronchial or perivascular connective tissues. No appreciable fibrous and reticular reaction of the interstices against the intrusion of the soot dusts could be detected except in the walls of the above mentioned alveoli which were distinctly filled and crumbled with the penetrated soot dusts, where a slight latticed fibrous growth and an initial minimal aggregation of such fibers could be seen. Otherwise, no proliferation of the connective tissues attributable to the presence of the soot dusts were observable.

The soot deposition in the intra-pulmonary lymphatic follicles presented the identical appearances to those seen in the cortical nodules and in the surroundings of the lymphatic nodules of the pulmonary hilus, a subject to which we shall revert to later.

How can this remarkable fact of the settlement of soots in colonies accompanied by the thickening of the walls be explained? Such alveolar groups were found localized often, if not always, in the lung sections where the agitation of their respiratory action, the self-purifying processes, was most likely to take place, the sub-pleura, peri-bronchial and perivascular parts However, in one instance the authors noted the existence of such a colony which had in no way any immediate connection with the pleura, bronchi or blood vessels. Now, if some of these alveolar cavities were fully packed with numerous dust cells or free soot dusts, it should be difficult for the self-purifying action to take place because of the curtailed freedom of the respiratory movement. If such were the case, the soot dusts would remain in the alveolar cavities as a sort of harmless foreign substances. And if those foreign substances no longer need to be purified or resorbed, then it is quite understandable that they should tend to remain settled or capsulated. In the same sense the soot packed alveoli tended to aggregate in order to embody the soot dusts as a sort of self-protective function of the lungs. It is also undoubtedly advantageous that the wall of such alveoli should be appreciably thickened so as to hinder the otherwise free respiratory action of the alveoli. Such

[illegible] that the soot [illegible] should be found [illegible] rest of the [illegible]. [illegible] sent [illegible] in the [illegible] walk of [illegible] peculiar [illegible] sentiment [illegible] [illegible] protection [illegible] the [illegible] [illegible] [illegible] [illegible] such [illegible] [illegible] [illegible] were [illegible].

The [illegible] in the [illegible] [illegible] cortic [illegible] nodules of the [illegible] revert to [illegible].

[illegible] of the settlement of soot [illegible] colonies [illegible] by the [illegible] of the [illegible] not [illegible], in the [illegible] [illegible] [illegible] [illegible] of [illegible] [illegible] of the [illegible] such [illegible], the [illegible] would [illegible] [illegible] a sort of [illegible] foreign [illegible] if those [illegible] no longer [illegible] to the [illegible] [illegible] it is quite understandable that they [illegible] had to [illegible] or organized. [illegible] tended to regard [illegible] in order [illegible] the soot [illegible] as a sort of self-[illegible] lands. It is also undoubtedly [illegible] should be [illegible] the [illegible] [illegible] of the [illegible]

[illegible] 10, [illegible] subject: "[illegible] [illegible]," [illegible]

thickened walls are composed of highly proliferated alveolar epitheliums, sporadic histiocytes, fibroblasts and neutrophile leucocytes. The somewhat premature appearance of the proliferated epitheliums witnessed in the case of Animal Number 86 is easily understandable when compared with the appearance of pneumonia colonies which brought about by the linear proliferation of the alveolar epitheliums resulting from the functional disorder through the intra-alveolar infiltration.

How did this infiltration, namely the proliferation of histiocytes, fibroblasts and neutrophile leucocytes come about? No doubt this process may be interpreted as a form of the protective function of the lungs, but on the other hand, this same process will facilitate further deposition of soots in the interstitial tissues by way of the lymphatic circulation. It was observed in all the specimen sections of the lungs that the penetration of the soot dusts into the alveolar wall took place most intensely. As for the neutrophile leucocytes, the authors have already observed earlier that the soot dusts could bring about a relative infiltration of such leucocytes. The sporadic proliferation of the reticulars and fibro-blasts must be one means of reaction actuated by the infiltration. This finding in the experimental anthracosis is of an utmost significance in indicating the most likely route through which the soot dusts penetrate into the interstitial tissues. In order to determine the possible role which soot deposition may play in human anthracosis, the authors examined approximately 300 sectional specimens of the lungs, arbitrarily selected, and found only 3 cases in which indentical form of soot deposition was observed. This led to inference that this type of soot deposition occurs only where dusts are raised intensely under controlled experimental conditions; hence it should play a relatively minor role in the case of protracted human anthracosis incurred through relatively milder dust concentration.

(2) Symphatic Nodules of the Pulmonary Hilus:

The lymphogene migration of the soot dust, once filtered into the lung interstices, takes place fairly promptly. AKAZAKI found that sporadic deposition of soots appeared in the lymphatic nodules of the pulmonary hilus after 8 hours of inhalation and grew to a very pronounced degree in the next 24 hours. In the present experiment, soot particles began

to appear both in the sinus and in the medullary and cortical perenchymas after 16 days (Animal Number 86). Soot particles were present very sporadically in the sinus, either ingested by the endothelial cells or in the free state. The soots were ingested by the reticular cells and sporadically settled in the medullary cord and cortical tissues. Particularly distinct soot deposition was observed around the cortical nodules, especially on the side lying close to the outlying sinus.

The amount of soot dusts present in the lymphatic tissues increased with the length of the experiment, especially around the cortical nodules or in the medullary cords. Such soot dusts readily aggregated to form an enormous mass. This mass of soot was mostly intracellular and partially extracellular, just like the soot packed alveoli previously mentioned. The soot ingested cells were, no doubt, derived from the reticular cells and assumed the form of gigantic cells when the soot dusts were strong. Intercellular and free soot depositions were found in the lymphatic parenchymas. When the experiments were continued over an extended period of time, as in Animal Number 7, the soot deposition in the lymphadenoid tissue grew to such a pronounced degree as to present an almost diffusive deposition. In this case, the soot-ingested reticular cells grew enormously both in size and number, but neither was the interstitial growth of the lattice, the aggregate fibers scarcely noticeable, nor did the soot dusts give rise to fibrosis.

The deposition of soot presented an entirely different picture in the case of the cortical nodules; namely, the soots were found settled around the nodules, especially in a pronounced state in their inner sections, which then later spread to all parts enclosing the nodules as the deposition grew. However, the soots were seldom present inside the nodules, but scattered or ingested in the reticular cells. In the sinus, contrary to expectation, the soots seldom appeared and if so, they were found very sporadically imbedded either in the free state in the peripheral and medullary sinus or ingested by the endothelial cells. Only when the experiment was conducted for a long period of time, as in the case of Animal Numbers 19 and 7, the lumphatic parenchymas were appreciably affected through soot deposition and the phenomena became distinct.

(3) Other Organs:

With an effort to determine the metastasis of the soot dusts within the body, the authors histologically examined the spleen, liver, kidney and the bone marrows, but no convincing evidence of such transference of soot dusts to other organs was discovered.

4. Summary and Evaluation of Experimental Results:

The objective of the present experimental research on pulmonary anthracosis by using rabbits as test animals was two-fold; firstly, to make an accurate analytical study of the lungs affected by inhalation of various types of dusts and secondly, to probe into the pertinent problems thus far unexplained.

From the intense dust (oil soot) inhalation test conducted with rabbits, the authors have discovered the remarkable appearance of the alveolar groups fully packed with soot dusts accompanied by distinctly thickened walls and a pronounced state of their atrophy. This phenomena must be considered as sort of protective processes of the lungs called into action against the intrusion of soot dusts which were actually found firmly embodied in the atrophied lung alveoli. But, it is easily conceivable that a portion of the soots lying in a free state inside the alveoli should pass into the interstices by way of the lymphatic circulation. Concerning the mechanism by which the soot dusts penetrate into the lung interstices, nothing conclusive can yet be said, but it appears highly probable that the soot dusts are admitted into the interstices in a free state. The alveolar epitheliums participate first in the thickening of the alveolar epitheliums and then followed by the reticular cells and the connective tissue cells. A moderate proliferation of the lattice fibers and the infiltration of neutrophile leucocytes were also observed. The distinctly visible lining of the inner phases of the alveoli and the alveolar epitheliums must have been affected as a result of the alveolar cavities being plugged with soot dusts, which the authors believe remain in the free stable state. Consequently, the epitheliums absorbed very sparse amount of soot dusts, if any. The authors are yet in no position to say anything conclusive with regard to the organization of the soot dusts found packed inside the alveoli.

The metastatic deposition of soot dust in the lymphatic nodules of the pulmonary hilus was observed to commence first with a sporadic migration in the cortical nodules and the medulla mostly ingested by the reticular cells or settled in a free state in the tissue crevices. In the course of time, however, the soot dusts gradually tended to assemble in masses on

the inner brim of the cortical nodules or in the medullary cords. In the case of prolonged experiments, the deposition of soot dusts accumulated to a pronounced degree and was soon found aggregated into piles all over the lungs. As a rule proliferation of lattice and connective tissues fibers were not observed. Hence, it may be concluded that the presence of soot dusts appeared from the start, sparsely if not in any pronounced degree, in the peripheral and medullary sinus and they persisted in the same state until fairly later date, even in the case of the longer experiments. When the soot dusts appeared in a pronounced state in the lymphatic parenchymas, soot dusts were found in the peripheral and medullary sinus, either in the free state or ingested by the endotheliums.

The assembling of the soot dusts in the cortical section around the cortical nodules, especially on its inner surface, can be explained by the plasma-eruption theory of Professor ONO. The haematogenc migration of soot dusts to remote organs of the body was extremely difficult even at high concentrations of dust inhalation.

EXPERIMENTAL RESEARCH ON THE
PATHOGENESIS OF SILICOSIS

By

Sumito TAKEUCHI

Department of Pathology,
Niigata Medical College, Niigata

ABSTRACT

(Published in the Journal of the Hokuetsu Medical Association, 59, 306-327 (1944).

1. Introduction:

Numerous detailed accounts of the pathological, anatomical and histological researches on silicosis have been conducted all over the world, but little has been known about the initial stage in the development of the disease other than that reported by AKAZAKI and GARDNER. The present research is to determine the likely region where the silicotic tubercles are first formed and the form of their growth. Once this is known, the genesis of silicotic tubercles and the structure of the normal alveolar walls can be understood.

2. Experiment:

The experiment was divided into two parts; inhalation test and injection test. Rabbits were used as the experimental animals.

a. Inhalation Test:

(1) Experimental Animal: Eighteen young healthy rabbits, strong enough to withstand a prolonged test, were selected for the experiment which was conducted for a minimum period of 4 to a maximum of 40 months.

(2) Silica Dust: The silica dust used for the experiment was prepared by the laboratory of Asano Cement Manufacturing Co., and its chemical composition was 95% SiO_2 and very small amounts of Al_2O_3, Fe_2O_3, CaO, MgO, etc. The size of the dust particles was 50 to 60% below 5 μ.

Incl 11, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

(3) Experimental Method: Two or three rabbits were placed in a specially designed cage into which dried silica dust was admitted for 30 to 60 minutes per day by means of a dust blower. The rabbits were left in the cage for 10 minutes after the blowing was suspended. In this manner the animals were forced to inhale dust for 40 to 70 minutes period daily. The length of the inhalation period varied each day depending upon the season and the health conditions of the animals. Care were taken to allow the animals to survive the experiment as long as possible. Finally, they were killed and their lungs and other internal organs were macroscopically and histologically examined.

(4) Experimental Data: The experimental periods, frequency of the forced inhalation and the weight of the animals before and after the experiment were recorded and summarized in the following table:

TABLE I.

Test Animal Number	Body Weight		Duration of Experiment		Number of Inhalation	Nature of Termination	Macroscopic Observations
	Commencement, g	Termination, g	Inhalation Period days	Period after last Inhalation days			
45	1500	2350	118	none	89	died	No conspicuous change
44	2200	2350	119	none	117	died	"
128	2655	2860	263	none	145	died	"
120	2400	2650	265	none	121	died	"
121	2900	2195	265	none	121	killed	"
46	1520	2330	347	62	165	died	Engorgement and Haemorrhage
110	2175	1600	359	none	179	killed	Macroscopic changes not perceived.
47	1555	2350	479	none	184	died	Lungs and other internal organs engorged (Bronchial pneumonia)
108	1570	2300	493	62	204	died	Serious bleeding in lungs
122	1850	2575	523	62	208	killed	Bleeding in lungs; no other changes
127	2750	2670	556	62	229	died	No changes other than bleeding in lungs

TABLE 1 CONT'D

105	2020	3030	716	none	271	killed	Other than 2 large abscesses in left lower lobe, no changes
[illegible]	1[illegible]0	2[illegible]50	810	none	242	killed	Large abscess in abdominal cavity, no changes in lungs
150	2210	2910	825	183	293	killed	Silicosis ganglions as large as millet seeds developed in lungs
109	1700	2310	968	none	239	killed	Greyish white silicotic tubercles formed over entire pulmonary lobe
24	2200	3005	1057	none	242	killed	No macroscopic changes
102	1985	3050	1237	214	334	killed	"

(5) Experimental Observations:

(a) Pathological processes typical of silicosis were developed in the pulmonary hilus area.

(b) Most of the silica dust that had been inhaled and reached the alveolar cavities after being first resorbed by the alveolar phagocytes appeared to be expectorated mostly in the free state. A portion of these phagocytes that ingested the silica dust seemed to crumble and disappear inside the alveoli, but some of them were found to persist in some alveoli, specially in a pronounced degree near the bronchial walls. The dust cells were never seen to grow into silicotic tubercles even after remaining in the alveoli for a long period. Wherever the silicotic tubercles appeared, the initial stage always took the form of large proliferated phagocytes filled with silica dust and then gradually collagenized after developing distinct lattice-form fibers around themselves and finally passed into hyaloid tubercles. The infiltration of polynuclear leucocytes or lymphocytes seldom takes place in this process. For silicotic tubercles to develop, it is always necessary that the silica dust should first penetrate into and settle in the inter-pulmonary substances.

Opinions as to how the metastasis of the silica dust takes place after filtrating into the interpulmonary substances differ among the past researches. The evidences found in this experiment show that the inhaled dust penetrates into the inter-pulmonary substances and is always carried off in the free state based upon the following reasons: 1) the so-called dust cells embodying the silica dust are seldom found in the alveolar walls; 2) the alveolar areas are the least likely place for the appearance of the tubercles; and 3) the alveolar walls are generally too thin to allow metastasis of large phagocytes along the alveolar lymphatic duct, which is not large enough for this purpose.

(c) The most likely place for silicotic tubercles to appear has been proved experimentally to be outside the blood vessels, peri-vascular alveolar walls, and peri-bronchial lymphatic follicles. Next to these areas were the sub-pleural and peri-bronchial sections. It is very seldom that silicosis should appear elsewhere, that is, in areas unconnected with blood vessels or bronchi.

(d) After the dust filtered into the inter-pulmonary substances and deposited, the fine reticular cells were proliferated by ingesting the dust. Then the lattice-form fibers were proliferated and finally produced hyaloid tubercles, pronouncedly removed of blood vessels, through collagenization. In this process, fibrous granulation cells and connective tissues were seen to take part in the development of the tubercles, but they are of secondary significance. Infiltration of poly-nuclear leucocytes and lymphocytes seldom occurred as these migratory cells do not assist in the formation of the granulations.

(e) The pathological process always takes place, mainly in the medulla, in the lymphatic nodules of the pulmonary hilus areas. Dust ingested reticular cells first proliferate into the medulla where the lattice-form fibers grows and finally becomes collagonous.

b. Injection Test:

(1) Experimental Animal: Eight rabbits, each weighing approximately 2500 g, were employed as the test animal.

[illegible] thought to be the precursors of the [illegible] have been [illegible] after filtering into the [illegible] [illegible] the [illegible] measurement. The evidence [illegible] [illegible] along the [illegible] dust [illegible] with [illegible] and is [illegible] [illegible] They [illegible] have the following reasons: 1) the [illegible] that cells [illegible] the silica dust are [illegible] found in the alveolar walls; 2) the alveolar areas are the most likely [illegible] give the appearance of the tubercles; and 3) the alveolar walls are generally too thin to admit [illegible] [illegible] the alveolar lymphatic [illegible], which is [illegible] large enough for this purpose.

(b) The most likely [illegible] for silica to [illegible] has been [illegible] [illegible] to [illegible] the blood vessels, [illegible] [illegible] and [illegible] [illegible]. [illegible] [illegible] the [illegible] [illegible]. It is very [illegible] that [illegible] [illegible], that [illegible] is [illegible] [illegible] with [illegible].

(c) After the [illegible] into the [illegible] [illegible] and depositing, the [illegible] cells were [illegible] [illegible] the [illegible]. Then the [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible]. [illegible] [illegible] cells [illegible] [illegible] in the development of the [illegible], [illegible] [illegible] significance. [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] in the [illegible] of the [illegible].

(d) [illegible] always [illegible], [illegible] [illegible] nodules of the [illegible] [illegible]. [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] [illegible].

[illegible]

(1) [illegible] : [illegible] [illegible], [illegible] [illegible] [illegible] to the [illegible] animal.

[illegible]

( ) Injection Fluid: The injection fluid was prepared by emulsifying physiological saline solution with 2.5% of the same finely pulverized silica dust used in the inhalation test.

(3) Experimental Method: The emulsion was injected into the auricular vein of the rabbits at the rate of 2 to 3 cc/kg. of body weight at intervals of 1 week, while care was taken not to injure the animals so that repeated injects could be carried out as many times as possible. However, due to injuries sustained by the auricular veins, the injections could not be repeated over 24 times. The duration of the experiment was from 2 months to 12 months. After the injections, each animal was kept alive for different period of time and then killed for the purpose of macroscopical observation of the organs.

(4) Experimental Data: The details of the experiment are tabulated in the following table:

TABLE II.

Test Animal Number	Duration of Experiment, months	Duration after last injection, months	Number of Injections	Body Weight Commencement, g	Body Weight Termination, g	Nature of Termination
58	2	1,5	2	2050	2350	Killed
57	2.5	1,5	4	2200	2880	"
56	7.5	3,5	7	1910	2200	died
52	5	1	11	2760	2280	"
54	12	2	14	2340	2840	"
50	12	2	24	2650	3250	"
53	12	2	24	2545	3420	"

(5) Experimental Observations:

(a) The liver was most pronouncedly affected. Most of the silica dust injected into the animal were ingested by Kupffer's asteroid cells, which are consequently enlarged, incurring the proliferation of the lattice-form fibers in their surroundings and giving rise to cicatrices where the granulated tissues had developed. Thus, enormous

silicotic cicatricial tubercles grew in the liver, resulting in a hepatic induration of a peculiar type. During this process, however, no collection of ascites was detected in spite of the intensity of the process.

(b) Nodules were formed around the coarse silica dust particles which had plugged the alveolar walls in the lungs and the appearance of the enormous cells. Sometimes silicotic tubercles, similar to those observed in the inhalation test, were developed due to the deposition of the silica dust which had filtered in along the lymphatic duct.

(c) Silicotic tubercles are formed in the medulla and the lymphatic follicules in the spleen. However, such tubercles are absent in the sinus. The tubercles are formed in the medulla of the bones on rare occasions but to a very slight extent. The lymphatic nodules, even those existing in the pulmonary hilus area, are affected in the same way as in the case of the inhalation test, but the degree of the pathological process was far less pronounced.

3. Conclusions:

a. It has been experimentally proven that all the dust penetrating into the body of the rabbits either by forced inhalation or injection was conjested by the cells of the reticular endothelial series giving rise to the proliferation of the lattice-form fibers, which are collagenized and finally resulted into typical silicotic tubercles. Sometimes the proliferation of the fibrous granulation cells and the connective tissues were involved in the process, but they must be regarded as only of secondary importance. As a rule, the participation of the lymphocytes and poly-nuclear leucocytes in the granulation process was not observed.

b. The finer silica dust particles are more conducive to the development of silicosis due to the fact that finer particles can readily filter through the alveolar walls and transferred to other parts of the body.

CONTRIBUTION TO THE SUUDY OF
HUMAN PULMONARY ANTHRACOSIS

By

Dr. Fujio NITTONO, Department of Pathology, Niigata Medical College, Niigata

ABSTRACT

(Published in the Trans. Soc. Path. Japan, 30, 290-296 (1940)

Though the problem of pulmonary anthracosis has been constantly studied for over a hundred years, there still remains many unclarified points which await further investigation. The following is a report on the noteworthy results of the author's systematic macroscopical and histological examination of the 108 autopsy cases performed on the human lungs affected by inhalation of coal dusts.

1. Macroscopic Examination:

a. The Degree of the Coal Dust Deposition in the Lungs: To determine the amount of coal dust particles deposited in the lungs, the author visually examined the coal dust particles deposited in a certain unit space on the surface and sectional specimen of the lungs.

(1) Comparison of the Degree of Coal Dust Deposition in Both Lung Lobes: Among the 69 cases examined, almost the entire group (66 cases) showed no marked difference in the coal dust deposition between the right and left lungs. Although the bronchi of the human lungs are not anatomically indetical, such difference is apparently attributable to the fact that the human being inhales only a small quantity of dust particles during his normal daily breathing.

(2) Comparison of the Coal Dust Deposition in Each Lobe of Both Lungs: The amount of dust deposition, both in the upper and lower lobes of the human lungs, is for the most part approximately the same as shown in Table I for the left lung and Table II for the right lung.

TABLE I-LEFT LUNG

Where Upper Lobe of Lung was more Strongly Affected than the Lower Lobe	Where Both Upper and Lower Lobes were Equally Affected	Where Lower Lobe was more strongly Affected than the Upper Lobe.
27 cases	35 cases	7 cases

Incl 12 Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates" dtd 15 Dec 48

TABLE II-RIGHT LUNG

Where the Upper Lobe was more Strongly Affected than the Lower Lobe	Where both Upper and Lower Lobes were Equally Affected	Where the Upper Lobe was Less Affected than the Lower Lobe
20 cases	35 cases	6 cases
Where the Lower Lobe was more Strongly Affected	Where Lower and Middle Lobes were Equally Affected	Where the Lower Lobe was Less Affected than the Middle Lobe
25 cases	43 cases	1 cases

The deposition of coal dust particles in the lung apex was not pronounced as shown in Table III.

TABLE III COMPARISON OF DUST DEPOSITION IN LUNG APEX

	Where the Lung Apex was More Affected than Other Parts of the Upper Lobe	Where the Apex and Other Parts of the Lung were Equally Affected	Where the Lung Apex was Less Affected than Other Parts of the Lung
Left Lung	9 cases	50 cases	18 cases
Right Lung	11 cases	49 cases	17 cases

The reports made by various authors on the results of their animal experiments and human data do not agree with regards to the distribution of the dust deposition with respect to each lung lobes. In most cases, the amount of dust deposited in each of the lung lobe was approximately the same, thus, the author concluded that each lung lobe inhaled approximately the same amount of dust particles.

(3) Comparative Study on the Dust Deposition in Each Pleural Phase of the Lungs: As a yardstick for the measurement of the coal dust deposition in the pleural phase, a pre-determined mass of dust particles visible on the pleural phases was used. Lungs with extensively thickened pleura were excluded.

It was noted in the majority of the cases, both in the left and right lungs, that the rib phases were most strongly pigmented, the mediastinal phases less strongly, the diaphragmatic phases still less, and the interlobar phases the least as shown in Table IV.

Lung	Where Rib Phases were More Strongly Pigmented than the Mediastinal Phase	Where the Rib and Mediastiral Phases are Equally Pigmented	Where the Rib Phase was less pigmented than the Diaphragmatic Phase
Left	51 cases	25 cases	1 case
Right	49 cases	26 cases	2 cases
Lung	Where the Mediastinal Phase was More Strongly Pigmented than the Diaphragmatic Phase	Where the Mediastinal and Diaphragmatic Phases were Equally Pigmented	Where the Mediastinal Phase was Less Strongly Pigmented than the Diaphragmatic Phase
Left	39 cases	35 cases	3 cases
Right	41 cases	34 cases	2 cases

The above mentioned differences in the degree of dust deposition in each section of the pleural phases must apparently be related with the degree of the mechanical resistance of each phase; hence the amount of pigmentation in the lobar phases is accountable by the relatively larger surfaces.

b. Different Forms of Dust Deposition in the Lungs: No adequate investigations have thus far been made regarding the different coal dust deposition on the pleural and sectional phases of the lungs. KREIPE has recently classified the forms of pigmentation into three principal forms, namely: network, string, and knot-form, which however, do not satisfactorily explain the different types of pigmentation observed in anthracosis.

After careful examination, the author analyzed the figures of the coal dust deposition on the lung surface and sectional phases. The figures were roughly divided into general types and special types of variation. The general type covered all deposition forms on the lungs and sectional phases is shown in Table IV.

TABLE IV

Phase	Type	Nomenclature	Description of Pigmentation
Pleural	1	Point-like Pigmentation	Figure as large as Pin-point
	2	Network Pigmentation	Figures resemblint network of lymphatic vessels
	3	Freckled Pigmentation	Pointed, round, or irregularly formed pigmentation larger than Type 1
	4	Diffusive Pigmentation	More or less diffusive pigmentation
Sectional	1	Point-like Pigmentation	(same as in Pleural phase
	2	Freckled Pigmentation	"
	4	Diffusive Pigmentation	"

The special types of pigmentation, which consisted of one or more of the above mentioned general forms but developed from special process, are group into two types, namely: (1) round or freckled forms which derived from the subplueral lymphatic glands and (2) band-form or string-like pigmentation which developed in t e intercostal spaces.

2. Histological Findings:

a. Histological Findings of Pulmonary Anthracosis:

(1) The coal dust particles inhaled by respiratory action are never absorbed by the bronchial epitheliums, but they proceed further down into the alveolar cavities. Such coal dust particles, as filtered into the alveolar cavities, are mostly ingested by the so-called dust cells and partly eliminated in the free state by the sputum. In regard to the essential nature of the dust cells, one may regard then as the so-called alveolar epitheliums, because there are alwa s present in the transitional forms between the dust cells existing in the free state in the alveolar cavities and the dust-ingested epitheliums adhered to the cavity walls.

(2) In regard to the volume of dust particles present in the alveoli, it is often noted that larger accumulation of dust particles are found in the pathologically altered lung than in the normal lung; namely, in such atelectatic alveoli with thickened walls, in the alveoli in which solitary tubercles have settled, or in the alveoli which are embedded in the callous tissues of the cirrhotic tuberculosis as well as in the highly thickened pleura. The amount of dust particles which remains in the alveoli is determined not only by the amount of dust particles inhaled, but also by the normal respiratory action of the alveoli themselves.

On the other hand, only a sparse quantity of coal dust deposition was found in the case of emphysematous alveoli. This may be accounted for chiefly by the fact that the dust particles in the exparede alveoli are free and more likely to be driven out with the sputum from the system. Even if numerous cells are accumulated in the alveolar and bronchial cabities and appeared to remain adhered to their walls, no organizing process of any kind were found to occur on the walls.

(3) The author was not able to prove experimentally anything conclusive with regard to the particular points or locations through which the coal dust particles might filter into the alveoli.

However, inasmuch as the coal dust particles were found present all over the entire peripheries of the alveolar walls of all sections, one may conclude that the dust particles filtered not only between the epitheliums as ARNOLD reported, but also through all parts of the alveolar wall excepting those parts of the walls which correspond to the outer membrane of the epitheliums.

(4) The coal dust particles reaching the alveolar walls are carried off through the lymphatic vessels and then for the most part ingested by the interstitial connective tissue cells and histiocytes or partly deposited in free state in the lymphatic vessels or in the crevices of the tissue. The deposition of coal dust particles is especially dense in the peri-bronchial, peri-vascular, and sub-pleural connective tissues.

(5) One thing to be noted especially concerning the coal dust deposition in the peri-bronchial, peri-vascular, and sub-pleural parts is that a portion of the dust particles are filtered from between the alveolar epitheliums into the neighboring alveoli in the case of the large accumulation of particles. However, if the alveolar epitheliums were carefully examined, it would be seen that these epitheliums had ingested the dust particles and were ready to emit the dust particles into the alveolar cavities.

(6) In regard to the existence of dust particles in the lymphatic system inside the lungs, the sub-pleural or peri-bronchial lymphatic nodules are reported by the past researchers, such as RUPPERT, ARNOLD, SCHMITTMANN-LUBARSCH, BORST, JEISS, GIESSE and others, to present an image in which the coal dust particles appear early or tend to deposit themselves, but such was not the case in the author's experiment. Contrary to past research works, the coal dust particles were rarely ever present in the sub-pleural or peri-bronchial lymphatic nodules and if they ever appear by chance, they will appear in the peripheral parts as an image around the lymphatic vessels.

(7) In the case of fairly pronounced case of anthracosis, the intravasation (infiltration into the veins) of the coal dust particles into the blood vessels having thin walls and more so into the vascular capillaries were observed to have taken place as well as in the case of the anthracosially pigmented lymphatic nodules. With regard to the penetration of the dust particles into the vascular capillaries of the lungs, thus far only KOOPMAN has made a remark concerning the graphite dust particles but no report has yet been made on the penetration of these dust particles into the lymphatic nodules.

b. <u>On the Remote Transition of the Lung Anthracosis</u>: Concerning the metastasis of the dust particles to the remote organs of the body, the author has proved experimentally by a careful examination of the state of coal dust deposition in the spleen, liver, heart, and kidney of test cases selected from the 108 human cases. The various mechanisms of development for the spread of the dust particles, though the opinions of other researchers differ, may be summarized as follows:

(1) Haematogene Metastasis (As a result of the breakdown of the anthracostic lymphatic nodules swollen with the lung vessels or as a result of the intravasation of the anthracosic pigments into the blood vessels of the lungs)

(2) Retrograde Lymphogene metastasis (metastasis caused by the lymph)

(3) Lymphogene (on the pulmonary hilus) followed by haematogene metastasis

Of the three possibilities mentioned above, neither the breakdown of the anthracosic lymphatic nodules in the lung vessels nor the lymphogene retrograde dust migration can sufficiently account for the metastasis of the coal dust particles into the remote organs in view of the negative results obtained in the authors experiments. Many researchers have regarded these two possibilities as rare or improbable cases.

As for the lymphogene-harmatogene development, no one is yet in a position to establish its probability through histological data. But in view of the fact that even in the case of highly anthracosically pigmented lymphatic nodules of the pulmonary hilus, the closer these nodules lie to the veins, the more easily the decrease in the coal dust deposit can be ascertained by macroscopial observation. It may not be incorrect to state that this is one of the possible means by which the dust particles disperse.

With regard to the last possibility increasing attention has been given, the haematogene development through the intravasation of the coal dust particles, into the blood vessels and even into the small vessels (veins) of the lungs. The author has witnessed the intravasation of the coal dust pigments not only in the small veins but also in the capillaries of the lung and in the lymphatic nodules of the pulmonary hilus. No noticeable difference was observed in the amount of coal dust particles penetrating between the individual capillaries and the veins. The penetration of the dust particles was more frequent into the capillaries than into the veins.

The migration of the dust particles to the remote visceral organs takes place mainly through the haematogene metastasis, which proceeds through the intravasation of the coal dust particles into the small vessels and capillaries of the lung and lymphatic nodules along the pulmonary hilus.

STUDIES ON THE DEPOSITION OF COAL DUST
IN THE HUMAN LUNGS AND ITS MIGRATION

By

Dr. Fujio NITTONO

Department of Pathology, Niigata Medical College, Niigata

ABSTRACT

(Published in Hokuetsu Medical Journal (Japan), 55, No. 4, 210-291 (1940))

The results of the author's research on anthracosis in 108 human autopsy are briefly tabulated in Tables I through VIII. The quantity and type of coal dust deposition in the lungs and adjacent organs are given. The symbol used in the tables for the degree of coal dust deposition are as follows:

- + very small quantity
- ++ rather small quantity
- +++ small quantity
- ++++ medium quantity
- +++++ large quantity
- ++++++ rather large quantity

TABLE I - INTRUSION OF COAL DUST PARTICLES INTO LUNGS AND CAPILLARY VESSEL OF PLEURITIC TISSUES

Intrusion of coal dust		Intruded Part (lung lobes)	Volume of Intruded Coal dust Particles	Intrusion of Coal Dust		Intruded Part (lung lobes)	Volume of Intruded Coal Dust Particles
Index No.	Degree of Deposition			Index No.	Degree of Deposition		
15	Light	Left bottom	+			Right center	++
		Right "	+	98	"	Right bottom	++
		Right center	+			Left top	++
22	"	Right bottom	++	99	Heavy	Left bottom	++
						Right "	+
35	Heavy	Right top	+	100	"	Left top	+
						"	+++
41	"	Left bottom	++	101	Light	Right center	++
		Right "	+			Right bottom	+++
60	Light	Right center	+	102	Heavy	Left bottom	+
69	"	Right bottom	+			Left top	++++
72	"	"	+			Left bottom	++++
79	"	Left top	+	103	"	Right top	++++
86	"	Right bottom	+			Right center	+++
		Left top	++			Right bottom	++
87	Heavy	Right top	++	104	Light	Right center	++
		Right bottom	++			Left top	+++
94	"	Left bottom	+	105	"	Left bottom	+++
		Right top	+			Right center	++
95	Light	Left bottom	+	107	Heavy	Left top	+
96	Heavy	Right bottom	++			Left bottom	++
						Right bottom	++
97	"	Left top	++	108	Light	Left top	+++

Incl 13, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 4[illegible]

TABLE II-DEPOSITION IN SMALL LYMPHATIC GANGLION AROUND BRONCHUS

Index No.	Degree of Anthracosis	Lobe with Small Lymphatic Ganglion	Volume of Coal Dust Deposited
5	Slight	left top	(-)
	"	"	(-)
6	"	right top	+
		left top	+
9	"	right center	+++
		left top	+
11	"	left bottom	+
		right top	+
		right center	+
12	"	right bottom	(-)
13	"	left top	+
		right top	+
		right center	(-)
		right top	+
14	Light	right center	+
16	Slight	left top	+++
		left bottom	++
18	"	left top	+
		right top	+
		right center	+
20	"	right top	+
24	"	right top	++
		right center	+
26	Light	right center	++
29	Slight	right top	++
		right bottom	++
31	light	right top	(-)
34	"	left top	+++
		right bottom	+

Incl #13, to Report GHQ, TID, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 December 1948

TABLE II-DEPOSITION IN SMALL LYMPHATIC GANGLION AROUND BRONCHUS (Cont'd)

Index No.	Degree of Anthracosis	Lobe with Small Lymphatic Ganglion	Volume of Coal Dust Deposited
35	Heavy	left top left bottom	+++ ++
38	Light	left bottom	+
43	Slight	right bottom	++
44	"	left top	+
46	"	left top right top left top	+ (-) ++
51	"	right center right bottom	+++ +++
53	"	right bottom	+++
54	"	left bottom	++
61	"	left bottom	+++
62	Obscure	left top right bottom	+ +
63	Slight	right center	+++
68	"	left bottom right top	(-) (-)
69	Light	right center right bottom	+++ (-)
72	"	right top right center	+ ++
73	Slight	left bottom right top	(-) (-)
80	"	left top right top	(-) +

Incl #13, to Report GHQ, TID, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

TABLE II-DEPOSITION IN SMALL LYMPHATIC GANGLION AROUND BRONCHUS (Cont'd)

Case No.	Degree of Anth-racosis	Lobe with Small Lymphatic Ganglion	Volume of Coal Dust Deposited
82	Slight	left top left bottom	+++ ++
84	Light	left top left bottom right top	(-) (-) (-)
87	Heavy	right center	++
94	"	left bottom	(-)
96	"	right center	+
97	"	left top left bottom right bottom	++ (-) ++
100	"	right center	+
103	"	left top right top right center	(-) + +
104	Light	right top right center	+ +
105	"	right top	+
107	Heavy	left top left bottom right bottom	+ + ++

TABLE III-DEPOSITION IN BRONCHIAL LYMPHATIC GLAND

Index No.	Degree of Anthracosis	Deposited volume of coal dust of lymphatic gland
15	Light	+ + + + + +
20	"	+ + + + + +
85	Slight	+ +
86	Light	+ + + + + +
94	"	+ + + + +
100	"	+ + + + + +

TABLE IV-DEPOSITION IN LYMPHATIC GANGLION BELOW PLEURA

Index No.	Degree of Anthracosis	Lobe with Small Lymphatic Ganglion	Deposited Volume of Coal Dust
14	Light	right center	+
21	"	right center	+ +
40	Slight	right center right bottom	+ + + + +
94	"	right center	+ +
100	Heavy	left bottom left top	+ + +
104	Light	left bottom	+ +
105	"	right top right bottom	+ + + + +

Incl #13, to Report GHQ, TID, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

TABLE V--DEPOSITION IN LYMPHATIC GLAND BELOW PLEURA

Index No.	Main lung disease	Degree of anthracosis	Lobe with lymphatic gland	No. of lymphatic gland	Deposited volume of coal dust in lymphatic gland
18	T.B.	Slight	left center	2	++++&+++++
16	Bronchial pneumonia	"	left top left bottom	1 2	++++++ ++++++&++++++
46	T.B.	"	right top	1	++++++
59	(-)	Light	left top	1	+++++++
74	T.B.	"	right bottom	1	+++++++
75	(-)	Slight?	right bottom	1	++++++
86	T.B.	Light	left top	1	+++++++
99	(-)	Heavy	left bottom left bottom	1 1	++++++ ++++++
102 102	(-) (-)	" "	left bottom right top right bottom	1 1 1	++++++ ++++++
107	(-)	"	right center	1	++++++

Incl #13, to Report GHQ, TID, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

TABLE VI - BLOOD VESSEL OF LYMPHATIC GLAND

Index No.	Lymphatic Gland Intruded by Coal Dust	Degree of Deposition of Coal Dust at Lymphatic gland	Volume of Coal Dust at Lymphatic gland
20	R.H.D.	Heavy	++
35	L.H D.	"	++
	B.D.	"	++
36	R.H.D.	"	+
		"	
41	L.H.D.	"	+
	B.D.	"	+
46	L.H.D.	Light	++
52	L.H D,	Heavy	+
	R H D,	"	+
77	B.D.	"	+
87	R.H.D	"	+
	B.D.	"	++
95	L.H.D.	"	+
	R.H.D.	"	+
97	L.H.D.	"	+
101	L.H.D.	"	+
	R.H.D.	"	+
102	L.H.D.	"	+
	R.H.D.	"	++
	B.D.	"	+
103	L.H.D.	"	++
	R.H.D	"	++
107	L.H.D.	"	++

Index No.	Lymphatic gland intruded by coal dust	Degree of deposition of coal dust at lymphatic gland	Volume of coal dust at lymphatic gland
2	L.H.D	Heavy	+++
3	L.H.D.	Light	++
	R.H.D.	Heavy	+
10	L.H.D.	"	++
	B.D	"	++
11	R.H.D.	"	++
16	B.D.	"	++
17	R.H.D.	"	+
19	B.D.	"	+++
20	R.H.D.	"	+++
22	R.H.D.	"	++
26	B.D.	"	++
28	B.D	"	++
35	L.H.D.	"	++
	R.H.D.	"	+++
	B.D.	"	+++
36	R.H.D.	"	++
	B.D.		++
41	L.H.D.	"	++
	B.D.	"	+++
46	L.H.D.	Light	+++
52	L.H.D.	Heavy	++
	R.H D.	"	+++
77	B.D.	"	+++
79	L.H.D.	"	++
	B.D.	"	+

REMARKS: L.H D. Left Lung Lymphatic Gland R.H.D. Right Lung Lymphatic Gland
B.D. Lymphatic Gland at Bronchial Bifurcation

Incl 13, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates, dtd 15 Dec 48

Index No.	Lymphatic gland intruded by coal dust	Degree of deposition of coal dust at lymphatic gland	Volume of coal dust at lymphatic gland
87	L.H.D.	Heavy	+++
	R.H.D.	"	+++
	B.D.	"	+++
88	L.H.D.	"	+
95	L.H.D.	"	++
	R.H.D.	"	++
	B.D.	"	+++
96	L.H.D.	"	+
97	L.H.D.	"	++
	R.H.D.	"	++
	B.D.	"	+
98	L.H.D.	"	+
	R.H.D.	"	++
	B.D.	"	++
99	L.H.D.	"	++
100	R.H.D.	"	+
	B.D.	"	++
101	L.H.D.	"	++
	R.H.D.	"	++
	B.D.	"	++
102	L.H.D.	"	++
	R.H.D.	"	+++
	B.D.	"	++
103	L.H.D.	"	++++
	R.H.D.	"	++++
105	L.H.D.	"	+
107	L.H.D.	"	++
	R.H.D.	"	+++
	B.D.	"	+++
108	L.H.D.	Light	++++

TABLE VII - VISUAL PHENOMENA OF COAL DEPOSITION IN ORGANS

Phenomena / Organs	Part in which Coal Dust Image was Seen		Size of Coal Dust Image		Volume of Coal Dust
	Surface	Sliced surface	Surface	Sliced surface	
Heart	+ unfixed	+ unfixed	+ {Pulverized or Micro-grain shape	+ {Pulverized or Micro-grain shape	little
Spleen	-	+ "	-	+ "	rather large amount
Liver	+ Many equivalent images at inter-acinus	+ Many equivalent images at inter-acinus	+ "	+ "	"

TABLE VIII - HISTOLOGICAL PHENOMENA OF COAL DEPOSITION IN ORGANS

Index No.	Degree of Anthracosis	Heart		Spleen		Liver		Kidney	
		Deposited region	Volume of coal dust	Deposited region	Volume of coal dust	Deposited region	Volume of coal dust	Deposited region	Vol. of coal dust
101	Light	-	-	Travecu-lae jinis (L) slight	Slight	Glisson's Sheath	Slight	-	-
103	Heavy	Connective tissue of intermedi-ate subs-tance	Small amount	Around the artery of travecula jinis; Around Follicle; Splenic pulp; Sinus	Rather much amount	Glisson's Sheat; Central venous wall; Kuppel's? cell	Rather large amount	Glomiform capillary endotheli um	
105	Light	-	-	Travecu-lae jinis	Slight	Glisson's Sheath	Slight	-	-
106	"	-	-	"	"	"	"	-	-

RESEARCH ON THE INFLUENCES OF SILICOTIC PROCESSES UPON THE PULMONARY TUBERCULOSIS

by

Setsugi SAKAI, Department of Pathology,
Niigata Medical College, Niigata

ABSTRACT

(Published in the Journal of Niigata Medical Association (Japan), 62, No. 1, 1-10 (1948)

A. Introduction

It is unanimously agreed among all medical researchers that the silicotic patients are more liable to contract pulmonary tuberculosis than others. And it is also pointed out by many researchers that the frequency of tuberculous complications in silicosis runs parallel with the progress of silicotic processes. However, it is still an open question what effect is actually exerted by silicotic processes or the presence of silica dust upon the tuberculous process. No convincing explanation has yet been offered on this problem. Many researchers argue that the presence of silica dust or silicosis makes the prognosis of tuberculosis worse. Their argument, however, often lacks valid clinical and anatomical re-examination. On the other hand, Professor ROESSEL and his co-workers, basing their arguments on morphological studies, went so far as to assert that silicosis exerted beneficial influence on tuberculosis, enabling it to cure itself by forming cicatrices. Such being the case, an immediate solution of the problem, silicosis vs tuberculosis, is one of the most important subject among the medical researchers.

B. Results of Examination of Human Cases

1. Data Used in the Present Research:

The data employed in the present pathological-anatomical and histological studies were taken from the corpses of 12 miners who died from silicosis (3 cases of common silicosis and 9 cases of silicosis complicated with tuberculous processes).

2. Clinical Observations:

A summary of the clinical data obtained from the investigation of the said 12 dissected cases and the supplementary data obtained from the examination of 84 silicotic patients who were working under the identical conditions are as follows:

Incl 14 Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

a. Subjective Symptoms:

Symptoms such as cough, sputum, difficult breathing, pain in the chest, and heart acceleration are said to increase when simple silicosis is complicated with tuberculous processes.

b. Objective Symptoms:

Absence of objective symptoms is pointed out by many students as characteristic of simple silicosis, and few physical symptoms generally accompany silicosis in which tuberculous processes developed. Some even reported the disappearance of wet rhonchus and respiratory sound.

The results of author's investigation of silicosis complicated with tuberculous processes are summarized as elongated expiration, dry rhonchus, pronounced frictional sound on auscu1ation, and short or dull sound particularly noticeable on percussion.

c. Pathological-anatomical and histological Observations

The pathological state of silicosis became considerably complicated with the appearance of tuberculous processes, the main features of which are summarized as follows:

(1) The adhered foci of silicotic processes: Silicotic granular nodules appears nearly symmetrically in the right and left lungs according to many researchers. But the adhered foci appears not always symmetrically, but often unbalanced and unsymmetrically in both lungs. In this experiment, the silicotic nodules appeared in the upper lung field of both lungs.

(2) Formation of hollows: The hollow is formed after the crumbling or softening of the hyaloid nodules as in tuberculosis and sometimes in silicosis. The hollows are formed most frequently in the upper lobes and frequently on the back phase of the lung regardless of whether or not tuberculous complication occurs. This pathological process is particularly noticeable and pronounced when the tuberculous complication is involved. However, the silicotic hollows are very small compared with those of tuberculous origin.

(3) Pulmonary emphysema: Pulmonary emphysema was observed in only one case of simple silicosis.

(4) Pleural Pathological Processes: Researchers point out that pathological process in the lung tissues caused by the deposition of silica dust gradually spread to the pleura and turning it into callous or adhered pleura. Opinions differ among researchers as to how these pathological processes are affected by the development of tuberculous processes. The author observed fibrous adhesion in simple silicosis cases and adhesive process highly developed in all the complicated silicosis cases. Apparently tuberculous complication accelerates the adhesion process.

(5) Pathological processes in Bronchi: Naturally the upper bronchus is first affected by the inhalation of dust. More than half of the cases examined, the appearance of suppurative bronchitis was revealed in both simple and complicated silicosis. The author was unable to reveal any bronchial dilatation in either simple or complicated silicosis as reported by other researchers.

(6) Pathological Process in Lymphatic Nodules of Pulmonary Hilus: The lymphatic nodules of pulmonary hilus are reported to undergo pronounced silicotic pathological changes simultaneously with the nodules of the tracheal branchings and bronchial lymphatic nodules before any pulmonary changes occur. Traces of defunct silicotic cicatrices were detected in the lymphatic nodules of the pulmonary hilus. This may be accounted for by the fact that the silica dusts which filtered through the entire lung tissues are collected in the lymphatic nodules.

C. Results of Animal Experiment:

1. Method of Experiment: The test rabbits were injected daily in the vein of the ear for a period of 30-39 weeks with silica dust emulsion and 20 weeks later with 0.05 mg-1.0mg of tubercle bacilli of bovine type. Some animals were given another injection of 1.0 mg of tubercle bacilli in another 20 weeks. At the end of the treatment, the animals were killed at different periods and their viscera were closely examined. Two healthy rabbits, unaffected with silicosis, were contaminated with tubercle bacilli in the same manner as controls. Details of the experiment are tabulated in TABLE I.

TABLE I

		Silica Dust Injection			Tubercle Bacilli Injection		Weight		
Rabbit Number	Total Duration of Experiment, weeks	Period, weeks	Number of Injections	Period between last injection and TB Treatment, weeks	Number of Injections and Quantity, mg	Period between injection and Termination, weeks	Initial, g	Final, g	Nature of Termination
1 (control for 71)					I 0.05 II 1.0	20	2160	1700	killed
71	87	39	26	20	I 0.05 II 1.0	20	2820	1410	killed
2 (control for 79)					I 0.05 II 1.0	2	2150	3320	killed
79	74	30	26	25	I 1.0	2	3180	2670	died
80	56	39	26	20	I 0.05	6	2275	2180	died
50	47	30	24	20	I 0.05	4	2280	1550	died

2. Results of Experiment: The macroscopic findings were as follows:

Lungs: The tubercles in the lungs of the test animals were found to be larger than those of the control group and showed tendencies of adhesion process.

Spleens: The spleens of test animals were swollen to a pronounced degree and showed presence of large tubercles.

Lymphatic Nodules: The test animals showed somewhat swollen lymphatic nodules, but no tubercles were observed macroscopically in either group.

The histological findings were as follows:

Tubercules: The existence of tubercles was sporadic and about the same in number in both groups. The tubercles presented as aspect of chiefly epithelial cellular tubercles with an occasional appearance of Ranvier's gigantic cells in the control animals. These tubercles were coated with films of connective tissues having a highly infiltrated lymphocytes and their centers were often found disintegrated and softened with occasional image of cretaceous transformation. A somewhat large amount of tubercle bacilli existed in the caseated areas, but few were found in other parts.

The tubercles were larger and showed more pronounced tendency towards caseation in the test animals; in some parts exudative process was observed in progress. Furthermore, the alveolar walls were thickened by the deposition of silica dust which added to the tendency of the tuberculous process to spread over the surrounding area. The epithelial cellular tubercles in the control group were present among the diffusively proliferated spleenocytes, where sometimes, if not too often, appeared gigantic Ranvier's cells and tubercle bacilli. The fine reticular cells in the test animals were proliferated so diffusively that it was sometimes difficult to distinguish between tuberculous from silicotic processes.

Lymphatic nodules: The lymphatic nodules showed only in the control animals diffusively proliferated epithelial cellular tubercles. Pronounced tuberculous process involving an extensive disintegration was observed in the test animals among the diffusively proliferated fine reticular cells.

Livers: The liver in the control group showed sporadic epithelial cellular tubercles in which gigantic Ranvier's cell occasionally co-existed with tubercle bacilli. The test animals showed extensively developed hyaloid silicotic tubercles, with numerous epithelial cellular tubercles existing among them.

EXPERIMENTAL RESEARCH IN PULMONARY SIDEROSIS

By

Dr. Koji TAKAHASHI, Department of Pathology,
Niigata Medical College, Niigata.

ABSTRACT

(Published in the Research Report of the Pathology Department, Niigata Medical College, (Japan), 60, 1-21 (1944)

1. Preface:

Human pneumoconiosis attributable to iron dust inhalation was first pointed out by ZENKER in 1867, and was later verified by MERKEL in 1869. But little has been known as to whether iron dust alone is sufficient to cause this disease or whether some other factors are involved.

Since no authoritative information is available on this subject, the the author set out to make a first hand pathological study of the disease by experimenting with rabbits. Iron dust was difficult to keep afloat sufficiently long in the air because of its heavy specific gravity. To secure a satisfactory experimental results, the author injected ferric oxide solution into the vein of the test animals's ear and examined how the injected iron dust particles affected the lungs and other organs.

2. Experimental Method and Results:

a. Inhalation Test:

(1) Method of Experiment: Thirty rabbits were placed in a specially designed cage, into which was admitted pure ferric oxide dust for an hour daily by a small blower. After the dust blowing was suspended, the animals were allowed to remain in the cage for about 10 minutes and then removed. At times the blowing had to be suspended because of the physical condition of the animals. It was also suspended during the hot or cold season or when the motor did not function satisfactorily. The experiment was conducted for 26 days in the shortest case and 914 days in the longest, The duration and the number of times the inhalation experiment was conducted are tabulated in Table I.

Tab 15, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

TABLE 1 INHALATION EXPERIMENT

Rabbit Number	Duration of Experiment, days	Number of Inhalation Periods	Period of Rest after Last Inhalation, days	Body Weight		Disposition of Animals
				Beginning of Experiments, g	At End of Experiment, g	
20	26	9	6	2060	2100	Died
18	34	14	1	2885	2660	Died
16	88	28	11	2525	2450	Died
28	140	24	35	2300	2400	Died
29	168	24	63	2100	2350	Died
30	170	24	65	2100	2540	Died
19	212	58	5	2460	2940	Died
5	239	72	5	1970	2770	Died
13	246	62	1	1710	2540	Died
2	324	68	4 hrs	2200	2620	Died
22	324	70	2 hrs	1900	3000	Died
24	324	70	3 hrs	2050	2810	Died
11	331	74	1	1280	2900	Killed
15	331	74	1	2660	3270	Killed
26	336	75	7	1300	1800	Died
1	351	88	1	1900	2880	Killed
6	351	88	1	2090	2840	Killed
10	351	88	1	2040	2880	Killed
21	361	80	8	1900	3100	Killed
25	361	82	10	1900	2400	Died
3	412	88	15	2100	2750	Killed
12	412	90	15	2200	2950	Killed
23	432	95	4	2000	2650	Killed
27	432	100	4	2100	2750	Killed
8	448	92	3	2090	2900	Killed
4	[illegible]	133	1	2390	3050	Died
14	664	185	2 hrs	1310	2900	Died
9	684	202	5 hrs	2050	2480	Died
17	731	200	5	2490	2500	Died
[illegible]	914	212	91	2330	2000	Killed

(2) Results:

(a) Condition of the animals while alive: Generally speaking, most animals behaved well throughout the

experiment. The animals usually gained in weight except those that died from complication by other diseases. H Hence, it may be assumed that the ferric oxide dust inhalation did not exert any specific harmful influence upon the normal growth of the animals. With regard to the rabbits' susceptibility to diseases after the inhalation of the iron oxide dust, no instances are known where the death was caused directly by the inhaled ferrice oxide dust.

(b) Summary of macroscopic and histological findings: The degree of iron oxide dust deposition seemed roughly co-extensive with the duration of the dust inhalation treatment. The peculiar shade of the iron dust appeared to fade steadily as the time progressed after the treatment.

b. Injection Test:

(1) Method of Experiment: Emulsion of 2% ferric oxide dust in saline solution was prepared for injection. Each rabbit was injected 5 cc of the emulsion through the ear vein, twide a week for a duration of 3 to 107 weeks, and the animals were killed at the end of the specified duration, Most of the animals were killed within 30 minutes after the last injection, but some of the animals were allowed to live for a long time after the last injection. The details of the experiment are tabulated in Table II.

TABLE II. INJECTION EXPERIMENT

Rabbit Number	Duration of Experiment, weeks	Number of Injections	Period after Last Injection	Body Weight		Disposition of Animal
				Before Experiment, g	After Experiment, g	
131	3	5	30 mins	2540	2800	Killed
133	3	5	30 mins	1800	1960	Killed
121	24	34	24 hrs	1880	1970	Died
129	24	34	30 mins	2430	2800	Killed
[illegible]	34	45	4 days	1730	2860	Killed
132	35	41	30 mins	2200	2500	Killed
126	39	43	30 mins	2190	3260	Killed
128	39	43	30 mins	2540	3500	Killed
130	39	43	30 mins	2590	3295	Killed
12[illegible]	78	94	30 mins	1700	3200	Killed
[illegible]25	83	89	30 mins	1900	3000	Killed
[illegible]	100	83	165 days	2310	3050	Killed
12[illegible]	107	94	166 days	2000	3400	Killed

[illegible] 1[illegible], Report TID, [illegible], APO 500, subject: "Locus of Impaction of [illegible]," [illegible]

(2) Condition of the test animals while alive: After the injection, all the animals showed no pronounced pathological symptoms. Animals gained weight like normal animals.

3. Summary and Discussion:

After a long animal exp riment extending over 2.5 years in which the rabbits were contaminated with iron dust either by injection or inhalation, the aut or has come to the conclusion that the lungs and lymphatic glands showed evidences of iron dust deposition, but no image of the hardened connective tissures were detectable. This contradictory to the views expressed by ZENKER but agrees with CARLETON's (1927) experiment. However, CARLETON was not definite in his argument against the harmfulness of the iron dust particles upon the health, presumably because his experiment was not cond cted long eno gh to secure satisfactory results as well as being influenced by the results obtained by earlier researchers.

In as much as no proliferation of the connective tissues was detected after a sufficiently long period of experiment, the author may be justified in sayi g that the ferric oxide dust particles are harmless to the living organism.

To make certain that sufficient ferric oxide dust particles would be absorbed by the test animals, both dust inhalation and injection of iron dust em lsion were conducted which enabled the author to examine the effect of the dust not only upon the lungs but also upon other internal organs.

Finding CARLETON's report lacking in the histological findings of his experiment as follows:

Briefly, the histological findings of the author's experiment coincides with the results obtained on experimental anthracosis conducted by Professor AKAZAKI (1941), who made rabbits inhale soot dust particles, and also the results of another experimentation conducted by the author with coal dust.

Upon a closer examination, however, one may notice a distinct difference in the reaction of the rabbit's lung tissues against the iron dust particles and the coal or soot dust particles, namely siderosis and anthracosis. In the case of anthracosis, coal or soot dust particles, are often found deposited in the lung tissues obstructing the group of cells lying closely together in the bronchi, around the blood vessels and in the sub-pluera. A pronounced contraction is always noted in the group of alveoli plugged with soot dust, or a fairly pronounced proliferation visible o on the alveolar walls. Such is not always the case with ferric oxide dust i inhalation. No doubt when iron dust particles are inhaled for a long period, some cases showed somewhat proliferated epithelial cells on the alveolar walls occluded with free ferric oxide dust particles, but to a far slighter

extent than in the case of anthracosis. When the test animals were allowed to live after the last inhalation of ferric oxide dust particles neither an image of the occluded alveoli nor permanent changes of the lung alveolar walls was detected. If any pathological processes occurred, they were healed and disappeared so completely that it was almost impossible to detect any traces of the occlusion. Hence, the conclusion is that ferric oxide dust particles, when compared with coal dust or soot dust, are far less harmful to the health of animals.

How does the ferric oxide dust particles inhaled into the respiratory system pass from the alveolar cavities into the interstitial substances of the lung? Professor AKAZAKI and his colleagues gave a detailed account of the course of the dust infiltration observed in their experimental anthracosis and the author shares their view that ferric oxide dust particles likewise are carried about in the free state by the lymphatic current. This view is borne out by the fact that the free iron dust particles are often found settled in the inter-tissue substances of the alveolar walls, bronchi, and blood vessels. Only a very small portion of the iron dust particles, if any, are seen ingested by the histocytes or connective tissue cells.

Macroscopically, the ferric oxide dust particles deposited in the lymphatic glands present a somewhat different aspect from that of anthracosis, but the difference lies only in the shade and histologically it is essentially identical with anthracosis. However, there is one important difference to be noted when compared with anthracosis, i.e.: the ferric oxide dust inhalation or injection brings about a far less dust deposition even when the experiment was conducted over a long period of time. There were no instances encountered in which the medullary substances were occluded with ferric oxide dust and no prolieferation of the lattice or connective tissue fibers was detectable.

The author made a painstaking study of the effect of the ferric oxide dust particles upon other internal organs, such as liver, spleen, and bone medullae, but found no positive evidence of the metastatis of the dust particles particles within them.

STUDY ON THE PATHOLOGICAL AND ANATOMICAL PROCESS OF PNEUMOCONIOSIS ARTIFICIALLY CAUSED IN GUINEA PIGS AND THEIR RELATIONSHIP WITH PULMONARY TUBERCULOSIS

By

Dr. Masao YAJIMA, Department of Pathology,
Nagoya University, Nagoya.

<u>ABSTRACT</u>

(Published in <u>Memoir of Pathology</u>, <u>10</u>, No. 1, 1-135 (1935))

<u>Objective</u>: The objective of this experiment was to study the pathological process of pneumoconiosis by subjecting guinea pigs to dust inhalation experiments.

<u>Experimental Material and Procedure</u>:

1. Test Animals: Guinea pigs were selected because they are easy to handle and highly susceptable to tubercle bacilli. A total of 103 guinea pigs (78 females and 25 males) were divided into 3 groups; 12 in the 1st group, 51 in the 2nd group and 40 in the 3rd group. The 1st group was used as control and no dust inhalation test was given. The 2nd group were given dust inhalation test while those of the 3rd group were given subcutaneous injection of tubercle bacilli after the dust inhalation test was conducted. After the animals died from natural death or were killed with ether anesthesia, their lungs were examined to observe the pathological changes.

2. Dust Inhalation Apparatus: Closed wooden cages designed by the author were used. The dust was stirred up by an apparatus which operated the bellows at 30, 50, and 100 rpm equivalent to wind velocities of 6-10, 10-15, and 15-29 m/sec, respectively.

3. Dusts Inhaled by Guinea Pigs: Approximately 500 g of dust were collected in two days from the streets in Nagoya City, Japan. The coarser particles were removed by sieving with a fine silk strainer. Approximately 156 g of the fine particles were retained and used in the inhalation tests.

The dust was found to be composed of the following substances: fine sand, clay powder, charcoal powder, coarse silica, pulverized fiber from clothing, tobacco and cigarette paper, match sticks, rinds of peanuts, hairs, cyprus and azalea leaves, straws, rubber powder, and orange and apple peelings. After removing the coarser ingredients by sieving, the remaining fine particles were ground into a mortar and chemically analyzed according to Direction No. 30 of <u>Pharmacopeia Japonica V</u>. The mean results are tabulated in Table I.

No. 16, Report, TID, GHQ, FEC, APO 500, Subject: "Locus of Impaction of Particulates", dated 15 Dec 48

TABLE I ANALYSIS OF DUST

Characteristics and Composition	Mean Values
pH	7.08 at 24°C
Moisture	0.703%
Ignition loss	6.87%
Total Nitrogen	0.163%
Specific Gravity	2.5
Substance insoluble in HCl	none
Mineral insoluble in HCl	none
Silicic acid soluble in HCl	none
SiO_2	83.1733%
Al_2O_3	6.0366%
Fe_2O_3	0.1103%
MnO_2	none
CaO	2.4956%
MgO	0.4098 %
Chloride	0.082%
K_2O, Na_2O, P_2O_5, SO_4, CO_2, and TiO_2 components	none

4. Frequency and Duration of the Dust Inhaling Experiment: The experiments were conducted under various conditions which are tabulated in Tables II, III, and IV.

TABLE II DUST CIRCULATION, 15-29 m/sec

Number of Experiment	1	2	3	4	5	6	7	8	9	10
Date of Beginning	1932 2/8	2/9	2/10	2/11	2/12	2/13	2/14	2/15	2/16	2/17
Total Amount of Dust, g	58.5	110	107	100	50	53	50	50	100	100
Amount of Dust Blown in, g	20	35	78	65	24	23	32	31.5	60	47
Time of Operation	1.5 hr.	1 hr.	1 hr.	1 hr.	25 min.	20 min.	15 min.	17 min.	30 min.	40 min.
Number of Animals used	5	5	5	5	3	3	3	3	3	3

When the experiment was repeated over 10 times, at wind velocity of 15-29 m/sec, the animals presented many pathological symptoms, such as appearing emaciated, anemic, loss of skin texture, and developing catarrhalic conjectivitis.

Encl 75, Report, TID, GHQ, FEC, APO 500, Subject: "Locus of Impaction of Particulates", dated 15 Dec 43.

TABLE III DUST CIRCULATION, 10–15 m/sec

Experiment No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Beginning of Experiment	1933 5/2	5/7	5/13	5/19	5/24	5/30	6/4	6/9	6/15	6/20	6/25	6/30	7/7	7/12	7/16	7/21	7/28	[illegible]/5
Total Amount of Dust, g.	50	50	45	55	42	58	41	5	5	6	20	22	21	23	24	25	24	18
Amount of Dust Blown In, g.	18	18	17	19	17	20	15	1.5	1.6	2	6	6	6	6	7	6	6	4.5
Time of Operation, min.	15	15	20	15	10	15	10	3	3	3	4	5	4	4	4	3	4	3
Number of Animals Used	5	5	5	5	5	5	5	3	3	3	2	2	2	1	1	1	1	1

When the experiment was repeated 3 times at wind velocity of 10–15 m/sec, the temperature of the animals rose to 39.5°C and at the same time the animals lost weight and vitality. After the 7th experiment the temperature suddenly dropped and many animals showed signs of paralysis in the anterior part of the body.

TABLE IV DUST CIRCULATION, 6–10 m/sec.

Experiment No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Beginning of Experiment	1932 10/29	11/8	11/15	11/22	11/29	12/6	12/13	12/17	12/21	1933 1/4	1/7	1/11	1/19	1/24	1/27	1/30	2/2	2/10
Amount of Dust Blown In, g.	5	3	4.5	5.5	5	3.5	7.5	4	5	5.5	7.5	5	6	6.5	5.5	4.5	5	8
Time of Operation, min.	5	5	5	5	5	5	5	5	6	6	6	6	6	6	6	10	6	7
Number of Animals Used	5	3	3	3	3	3	3	3	3	3	3	3	5	5	4	4	4	4

Experimental Results:

The pathological, anatomical and histological processes of pneumoconiosis artificially caused in the animals were examined and the results obtained are summarized as follows:

(1) The dust particles collected from the street contained small amounts of organic matters and the chief constituent was silicates (83.1733%).

(2) Guinea pigs were selected as test animals since they are known to be highly susceptible to tuberculosis.

(3) The bacillus injected animals were confined in cages and forced to inhale measured amounts of dust circulated at three different wind velocities. The amount of dust in each experiment amounted to about 41 to 100 g. The number of inhalation tests was from 1 to 24 times and the period of examination of the tubercle bacilli innoculated animals was extended over a period of 10 to 152 days.

(4) When the dust inhalation experiment was intensely conducted, greater loss of weight was rapidly observed. During the first 14 days of the experiment, the animals lost from 85 to 280 g. each. Their temperature rose in most cases to 39°C and as high as 40.7°C and prior to their death the temperature dropped to 35-36°C.

(5) The results of the pathological and anatomical examination of the tubercular animals, in which pneumoconiosis was artificially developed, may be summarized as follows:

(a) Whenthe dust was inhaled in rapid succession, a large amount of dust was intensely absorbed by the animals and caused high degree of engorgement or even haemorrhage. When the dust was inhaled under less intensity, the surfaces of the lungs showed deposition of dust as black spots in numerous points. In the slide sections, atelectatic heptization colonies were observed. In some cases brownish red or greyish white anemic infarction colonies were found in the lung lobes. The lung surfaces were affected in varying degrees, but the right pulmonary apex and the tip of the lower lobe of the right lungs were most affected.

(b) The size of the hearts was mostly normal. The livers, however, showed icterus and their surfaces were glossy in most cases. The kidneys showed almost no inflammatory changes and the two constituent parts were

clearly distinguishable from one another. The size of the organs was also nearly normal.

(c) Catarrhal changes were found in the gastro-intestinal tracts and where these changes occurred in a pronounced degree the gastro-intestinal capacity was reduced and mostly filled with gases.

(d) A microscopic examination revealed that no pronounced pathological changes occurred in the lymphatic vessels. Only the lymphatic glands in the pulmonary hilus were appreciably swollen. Also the spleen was found somewhat enlarged. The bladder usually contained 2 to 15 cc of clear urine and as a rule presented no catarrhal changes, but in a number of cases bladder catarrh of advanced stage containing turbid urine was detected. The animals often produced a profuse amount of mucous secretion or bled through the nostrils. In some cases haemorrage in the pleural cavity was noted and ascites was observed in isolated cases.

(6) The pathological and anatomical examination of the animals whose lungs developed pneumoconiosis first were given subcutaneous injections of tubercle bacilli revealing the following results:

The loss of weight was considerable. Profuse mucous secretion was found in their tracheae and scattered engorgements were found in the lungs. Numerous dark stains which were particularly pronounced in the regions near the diaphragm were found over the surface of the lungs and in the advanced stages they formed flecky streaks. On the slide specimens, diffused, yet distinct millet-like tubercles were found and the lung parcenchyma was atrophy and anemic in many cases. The hearts were somewhat hypertrophied and contained large number of bloodclots. The livers were swollen and slide specimen showed yellowish white-grey tubercles, generally as large as millet and in some cases as large as linseed. The kidneys were found to consist of soft substance and yet the two constituent parts were clearly distinguishable from one another. The stomach and intestines showed in most cases catarrhalic stained greyish white mucous membranes. The lymphatic glands in the neighborhood of the larynx were swollen to the size of lima beans and fused to form glandular masses. The milts were enlarged and embraced numerous millet-like greyish white tubercles. Nasal catarrh was evident. Small and large engorgements were observed in the thorax. The spot of injections de-

veloped cicatrices on the skin and disappeared in due course of time, but in many cases they developed on the spots granular tissues having ulcers of varying sizes or fistulous holes which were found by sounding to run deep into the ribs.

(7) The results of the histological examination of the pneumoconiosic lungs are summarized as follows:

The amount of the red blood corpuscles in the lung capillaries and the lymphocytes in the alveoli varied greatly among the animals but the variation coincided roughly with the intensity and frequency of the dust inhalation experiments. In those animals that inhaled dusts through five experiments, the small bronchial walls were found to have different thickness in different portions and their tracts were either dilated or narrowed and filled with a profuse amount of secretion. The desquamation of the surface epithelial cells of the mucous membranes was pronounced. The tract was often filled with round cells and dust cells. Animals that inhaled dust over 10 times showed considerable proliferation of the peribronchial connective tissues accompanied by the deposition of free dust particles. The intra-alveolar infiltration of round cells was generally intense and fibrous networks were often present. In many cases the alveoli were compactly packed with erythrocytes, round cells, and dust cells and the kernels of these infiltrated colonies were found necrotic in the pulmonary peripheries. The capillaries were filled with erythrocytes and sometimes haemorrhage occurred in their surroundings. The proliferation of the elastic fibers was evident in the adventitia of the small vessels and also in the peribronchial connective tissues. In many of these cases catarrhalic pneumonia was developed in the lungs; heptization colonies were often found revealing the presence of dust particles in the alveoli of animals undergoing more that 11 dust inhalation tests. The peribronchial connective tissues were proliferated in a moderate degree. The infiltration of the round cells occurred in a stripe pattern around the bronchi and the alveoli. Haemorrhage of the peri-capillaries was also pronounced and the erythrocytes were found disintegrated in that portion of the lung lying near the pleura. At this point the haemosiderins were often reduced into smaller particles and present in a free state in the alveoli. Dust cells, embodying the dust

particles, were found near the alveolar epithelium and sometimes found deposited on the peri-bronchial connective tissues. When the animals inhaled a large amount of dust by intensive breathing, a considerable mass of dust cells were found in the alveoli regardless of the frequency of the inhalation.

(8) The histological examination of the lungs of the guinea pigs that were subjected to the dust inhalation tests and tubercle bacillus injection.

There was a promounced infiltration of the round cells in the small bronchi, whose cavities were often occluded or more or less widened and revealing proliferation of the peri-bronchial connective tissues. As a result of partial bleeding, homogenously organized substances were brought into action in these regions. Numerous dust particles and dust cells were found in the bronchial cavities. Numerous erythrocytes were found within the alveolar septa and numerous desquamated epithelial cells whose mass often caused necrosis in the center of the alveoli were within the alveolar proper. Follicular tubercles were found in the engorged alveoli. The capillaries were packed with erythrocytes and their adventitia were more or less thickened. There was also a noticeable infiltration of perivascular round cells in the capillaries. When the animals were made to inhale dust particles frequently, the degree of proliferation of the connective tissues was higher and the proliferation occurred predominantly in the surroundings of the bronchi and its blood vessels. When the tubercular processes developed to a marked extent, the proliferated connective tissues became necrotic and the disintegrated connective tissues were filled with lymphocytes and erythrocytes. Where tubercular colonies had developed, the connective tissues were infiltrated with round cells and atrophied. The histiocytes which had ingested dust particles in the walls of the alveoli. Where the haemorrhage occurred to a great extent, haemosiderins were found either deposited on the alveolar cells or present in the alveoli together with the dust particles in the free state.

The pneumoconiosis lungs in which tuberculosis was caused by the injection of the germs were generally congestive, but those lungs in which intensive inhalation of dust particles was conducted were very anemic and the presence of small black knots were observed on their surface. These isolated knots consisted of round and dust cells and the walls of the surrounding blood vessels were en-

larged. An appreciable number of proliferation of the connective tissues were often observed, but they seldom constituted the tubercles. The elastic tissues which were proliferated in a net like form appeared also in the neighborhood of the small bronchi where numerous dust cells had collected.

(9) The results of comparison of the histological studies of the lungs of those animals which were given simple dust inhalation treatment and with those that were given dust inhalation and tubercle bacilli injection treatment alternately.

The pathological differences between the simple pneumoconiosis and pulmonary tuberculosis are as follows:

Microscopic studies of the two types of diseases revealed that certain similarity existed between them. The tubercles caused by the bacilli formed small knots resembling the lymphofollicles which consisted of a mass of lymphocytes, and the proliferation of the connective tissues of these knots was more pronounced than those of pneumoconiosis of equivalent degree. As a result of the frequent inhalation of dust particles, the tubercle foci either underwent caseous degeneration or formed caverns through the disintegration of the parenchyma. In the case of pneumoconiosis, the capillaries showed greater degree of engorgement and even haemorrhages when the animal repeatedly inhaled dust, but in the case of tuberculosis, the engorgement progressed gradually until it reached a certain point which corresponded to the engorgement of medium degree pneumoconiosis. When the dust inhalation treatment was conducted over 76 times, the tubercle foci became very anemic.

In the lungs in which only minor pneumoconiosis was developed, various pathological processes were observed, namely, slight engorgement appeared by the irritation of the alveolar epitheliums and small bronchi in the case of slight case of pneumoconiosis and slight haemorrhage occurred sporadically with the infiltration of the round cells in the medium case, but the dust cells appeared in the alveolar septa together with the erythrocytes upon the onset of pneumonia. The disintegration of the tissues was not very pronounced. In these lungs in which pneumoconiosis was combined with the subcutaneous injection of tubercle bacilli, the follicular tubercle knots appeared in the medium cases and developed to such an extent that they were found chiefly in the alveolar spaces and

in the peribronchial connective tissues together with the dust cells. The disintegration of the tissues were pronounced. The proliferation of the connective tissues were generally more advanced in the tubercular lungs than in pneumoconiosis.

In the medium cases of simple pneumoconiosis, haemosiderin was found present between the alveolar epithelial cells, but in the tubercular lungs, it was found deposited in the caseous residue of the tissues in which numerous dust cells were detected.

(10) Reviewing the numerous past works on the dust inhalation diseases, one will note that most of the authors dealt chiefly with the chronic interstitial pneumoconiosis as the subject matter. However, as described above, artificial pneumoconiosis was caused in the guinea pigs by allowing them to inhale street dusts over extended period of time (longest period extended over 152 days). It has been noted that within a short period after the commencement of inhalation, catarrhalic or fibrous pneumonia was developed and even pneumoconiosis developed.

(11) The study of the known literature on the subject shows that VIRCHOW believed that the black pigments of anthracosis entered from the outside and not through the medium of the blood vessels. THOMPSON, ZENCKER, TRAUBE, etc., on the contrary, asserted that the pigments were emanated from the blood vessels. The author reached the conclusion that the inhaled silicate particles reached the alveoli and penetrated into the blood vessels and capillaries. The dust cells are then transported from the small blood vessels by way of the lymphatic vessels into the lung-parenchyma and deposited in between the connective tissues as black pigments.

When the guinea pigs were given a medium treatment of dust inhalation, black dots appeared on the surfaces of their lungs and in the case of more intense dust inhalation, the surface of their lungs appeared as if numerous sesame seeds had been sprinkled.

(12) When a simple dust inhalation was repeated over 10 times, the proliferation of the connective tissues were observed in the small mass around the bronchi. When this treatment was conducted for 16 times, the same pathological processes were observed with pronounced disintegration of the tissues. When pneumoconiosis of medium degree was combined with tubercle bacilli injection, a pronounced proliferation of the connective tissues soon appeared but seldom capsulated the tubercles. Nevertheless, the

proliferation occurred chiefly around the perivascular and peribronchial regions.

(13) Pneumoconiosis is seldom caused by inhalation of pure organic dust particles, but it is easily developed in most cases through the inhalation of dust containing inorganic materials. These dust particles are found deposited in the desquamated cells in the bronchi, in the infiltrating round cells and in the erythrocytes, which left the blood vessels when haemorrhage occurred. The cells which have ingested the dust particles appeared in the alveolar spaces and in the case of marked development, the alveolar spaces are disintegrated and the dust particles are found in the free state. The tubercle knots are found chiefly in the connective tissues, which have been proliferated around the capillary bronchi, and present a follicular form containing small amount of Langhorn's gigantic cells. The deposition of dust particles is apparent and in most cases the presence of haemosiderins is detected in the tubercular lungs combined with highly developed pneumoconiosis.

(14) Fibrosis appears in a slight degree in pneumoconiosis, but it appears in a pronounced degree in the initial stage of the tubercular lungs.

The presence of the deposited silicates in the lungs aggravates the pathological state of the disease by promoting the proliferation which is liable to lead to very undesirable detrimental consequences.

RESEARCH ON CEMENTOSIS

Part II EXPERIMENTAL STUDIES PERTAINING TO CEMENTOSIS

By

Dr. Hiramasa SENDA

Department of Hygiene, Faculty of Medicine,
Nagoya University, Nagoya

ABSTRACT

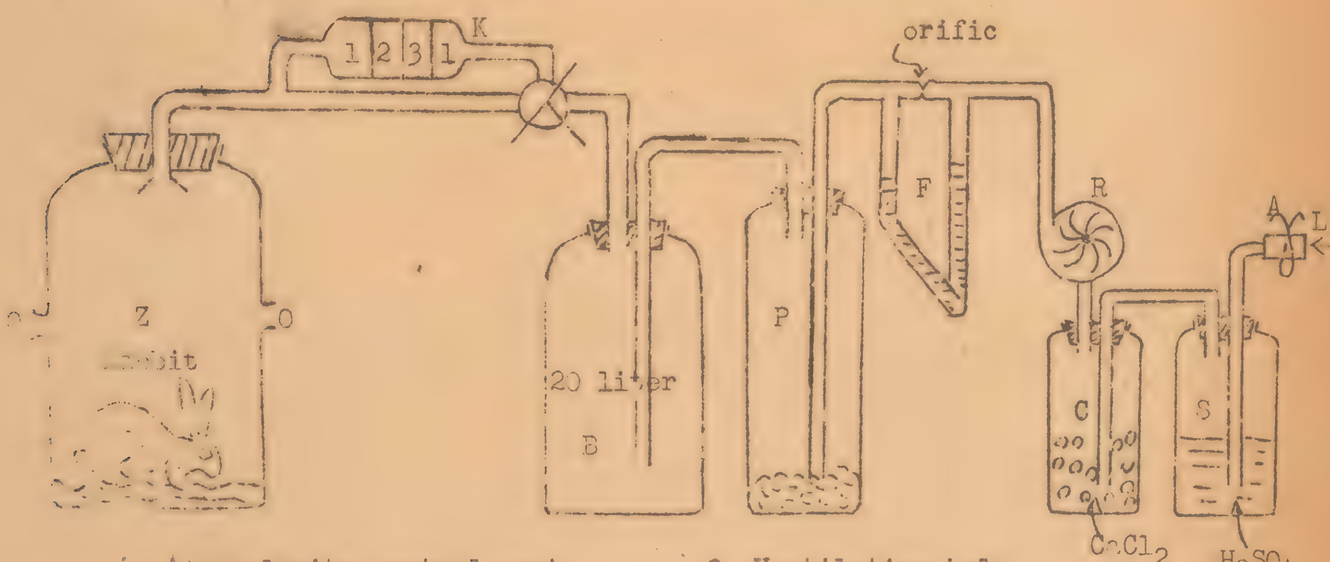
(Published in National Hygiene (Japan), Vol (?), 672-695 (1944)).

A. EXPERIMENTAL METHOD:

1. Dust Inhaling Apparatus: The Jotten and Arnoldi's Dust Inhalation Apparatus was employed, rather than other inhalators, because of its simplicity and accuracy in attaining the desired objective. The method was employed in this experiment with simplications as shown in Figure 1. There is one defect in this method, as well as in other apparatus, which is the non-stability of the floating dust particles under transmission. However, the dust inhalation experiment was performed as accurately as possible by regulating the velocity of the transmitted air.

FIGURE 1.

Experimental Apparatus for Dust Inhalation



A. Air velocity control cock
B Mixer bottle, 20 liter capacity
C Filter containing $CaCl_2$ powder
F Flow meter
K. Dust meter
L. Air inlet
O. Ventilation hole
P. Dust stirring apparatus
R. Rotary pump
S. Filter containing Concentrated H_2SO_4
Z. Inhalation chamber

Incl 17, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

The details of handling this apparatus are as follows: The velocity of the atmospheric air is regulated by pinch-cock, A. The air passes through filters, S and C, prior to entering the rotary pump, R, and then sent into the dust stirrer, F, at a constant velocity. The air containing the dust particles is introduced into a mixing bottle, B, to equalize the concentration of the dust particles to the proper level prior to its entrance into the inhalation chamber, Z. The inhaled air is blown out of the ventilation holes, O, installed on the side of the inhalation chamber. A rabbit is placed inside the inhalation chamber, Z, and allowed to inhale the dust particles for a fixed period. Filters, S and C, are provided to dehydrate the moisture in the atmosphere and to stabilize the stirred dust particles. K is a simple dust meter, which is filled with absorbent cotton (1), small glass beads (2) and sugar (3). The meter was calibrated by determining the difference in weight between the initial and final weighing. The author found that a 20 to 30% error occurred when compared with the "Impinger" method; therefore, an adjustment was made accordingly to adjust the amount of dust by an average of 25%.

2. The Type of Dust and the Concentration of Dust Particles: The type of dust particles and its concentration under transmission are tabulated in Table I.

TABLE I TYPE OF DUST PARTICLES AND ITS CONCENTRATIONS

Type of Dust Particles	Concentration of Dust Particles per cc	
	Maximum	Minimum
Cement	2880	1980
Calcium hydroxide	3600	2060
Silicon dioxide	1755	1404

3. Chemical Composition and Size Distribution of Cement Dust: The chemical composition of the cement dust used in this experiment is tabulated in Table II and the size distribution of the dust particles are tabulated in Table III.

TABLE II CHEMICAL COMPOSITION OF CEMENT

Component	Composition %
Insoluble Residue	0.33
Silicon Dioxide, SiO_2	22.23
Aluminum Oxide, Al_2O_3	6.25
Iron Oxide, Fe_2O_3	3.40
Calcium Oxide, CaO	65.06
Magnesium Oxide, MgO	0.77
Sulphur Trioxide	0.99
Ignition Loss	0.75
T O T A L	99.78

TABLE III SIZE DISTRIBUTION OF DUST PARTICLES

Type of Dust Particles	Size Distribution of Dust Particles by Percentage		
	Less than 1.0 μ	1.0 to 5.0 μ	Over 5.0 μ
Cement	10.5	56.5	23.0
Calcium Hydroxide	28.9	61.8	9.3
Silicon Dioxide	42.4	30.1	27.5

4. Test Animal and the Duration of the Dust Inhalation: The test animals used for this experiments were matured rabbits. The dust inhalation period for the rabbits was carried out for a period of an hour every day except holidays. The maximum duration of the dust inhalation for the rabbits was as follows: 345 hours for cement, 289 hours for silicon dioxide, and 1?7 hours for calcium hydroxide. For rabbits which had inhaled dust particles for about 6 months, a rest period of about 50 days was given and then the dust inhalation was continued. The total duration of the dust inhalation for each type of dust particles and the cause of death for each rabbit are recorded in Table IV.

TABLE IV DURATION OF THE DUST INHALATION

Type of Dust Particles	Commencement of Inhalation	Inhalation Suspended, days	Total Duration of Inhalation, hours	Cause of Death	Rabbit Number
Cement	30 Jan 41		50	Pneumonia	1
	31 Mar 41	53	345	Killed	5
	15 Apr 41		16	Pleuro Pneumonia	8
	20 May 41	52	185	Emphysema of Lung	10
Calcium Hydroxide	17 Feb 41		11	Dyspepsia	3
	3 Mar 41		23	"	4
	31 Mar 41		36	"	6
	15 Apr 41	20	187	Killed	9
	20 May 41	20	157	"	11
Silicon Dioxide	10 Feb 41		84	Pneumonia	2
	15 Apr 41		31	Dyspepsia	7
	22 May 41		8	Pneumonia	12
	22 May 41	53	289	Killed	13
	31 May 41		8	Pneumonia	14
	28 Jul 41		11	"	15
	8 Aug 41		35	"	18

B. EXPERIMENTAL RESULTS:

1. X-ray Observations: Although detailed pathological and anatomical observations in the experimental inhalation have been made in the past, no X-ray observations have been made. The observation of tuberculosis was made by JOTTEN and his colleagues in their experiment, but not for dust-lungs by means of X-ray. According to a recent report pertaining to silicotic lung by NAESLUND (1938), observation by X-ray was not successful due to the fact that the X-ray image of silicosis in rabbits or other animals are difficult to judge the size. Even the X-ray picture taken by the author were very difficult in distinguishing the detail changes. However, the occurrence of conspicuous characteristics due to the inhalation of various type of dust particles can be made by comparing the changes occurring in the lung field of the animals.

a. Rabbits Which Inhaled Calcium Hydroxide: X-ray pictures were taken of rabbit Numbers 4, 9, and 11 after 28, 30, and 85 days respectively, after commencement of dust inhalation. Either no changes were recognized in the heart and lung field (Numbers 4 and 9) or a slight shade was observed in the upper right and middle lung field (No. 11). This shade appeared clearly in the X-ray picture of rabbit No. 9 taken on the 121st day and indicated chronic bronchitis or broncho-pneumonia accompanied by obesity of pulmonary hilus and augmentated by the stripe-like shade. Bronchitis developed in rabbit No. 11 and was clearly noticeable as the duration of the inhalation progressed.

b. Rabbits Which Inhaled Cement Dust: According to observations of the X-ray pictures taken of rabbit No. 1 on the 40th and the 60th day after the commencement of inhalation, no change was observed in the picture taken on the 40th day, whereas a stripe-like shade occurring in radiation from the pulmonary hilus, together with an increase shade of the pulmonary hilus, as well as a steady obesity of the heart were observed on the 60th day. An observation of rabbit No. 5 was carried out by taking X-ray pictures on the 45th, 121st, and the 459th days after the commencement of inhalation. No changes were noted on the picture taken on the 45th day, but a shade in the upper and middle lung and obesity in the pulmonary hilus with conspicuous expansion of the heart were observed in the picture taken on the 121st day. A high degree of heart dilation appeared in the picture taken on 459th day, particularily on the right side which covered the shade in the pulmonary hilus. The stripe-like shade running downward combined and composed a wide band. Although the left lung field was almost invisible, except for the lower part due to the heart shade, a conspicuous shadow in the upper and middle lung field which presented a hive form were observed. Conspicuous shades of emphysema of the lung were observed in the right apex and lower field of the lung.

c. Rabbit Which Inhaled Silicon Dioxide: Rabbits Numbers 12, 13, 15, and 18 died within 40 days. Observations of the X-ray pictures of their chests showed images of bronchitis. However, the direct cause of rabbit No. 7's death was dyspepsia. Rabbit Numbers 2 and 13 managed to recover from the bronchitis without any attention or care. No evidence of bronchitis was observed in rabbit No. 2's picture on the 94th day. In the picture from rabbit No. 13 taken on the 77th day, a shadow was observed in the upper right and middle lung field. After 241 days, the shadow in the right upper and middle fields enlarged and extended to the lower lung field where the hive-like shade was observed. The stripe-like shade running downward from the pulmonary hilus increased remarkably in number and thickness with prolonged inhalation of dust particles.

In the X-ray picture of rabbits which inhaled silicon dioxide, special characteristics were observed as follows:

(1) In the early state of the experiment, silicon dioxide dust particles gave a comparatively harmful effect on the lungs, which developed into a chronic condition after the disappearance of the initial stage, and finally showed the characteristic silicotic lung shade.

(2) Slight heart dilation and no conspicuous appearance of emphysema in the lower lung field were observed.

2. Pathological Observation:

a. Macroscopical Changes in the Lungs: The details of the macroscopical observations of the lungs of dead or killed rabbits are tabulated in Tables V, VI, and VII.

b. Microscopical Changes in the Lungs: The microscopical changes observed in the lungs were similar to the macroscopical observations. The details are tabulated in Tables V, VI, and VII.

TABLE V PATHOLOGICAL AND ANATOMICAL CHANGES IN THE LUNGS OF RABBITS WHICH INHALED CALCIUM HYDROXIDE

Rabbit Number	Experiment Period and Duration	Duration of Dust Inhalation, hrs	Pathological and Anatomical Changes	
			Macroscopical Observations	Microscopical Observations
3	17 Feb to 2 Mar 41 (14 days)	11	No change on surface of lungs. Lungs elastic and bloody	Greater portion of lung system healthy except a small congested portion. Many dust particles in alveolar septa, but few dust cells. Dust cell in the blood vessel. Alveolar s pta, condensated
4	3 Mar to 30 Mar 41 (28 days)	23	Same as above	Same as above

6	31 Mar to 13 May 41 (44 days)	36	Several bloody and congested speckles on lung surface which were dark red color, but no other changes	Generally, lung tissue congested and an image of bronchitis appeared. Dust cells of medium size in the blood vessel. No free dust particles. A partial expansion of the lung in the state of emphysema
9	15 Apr to 13 Dec 41 (242 days) Inhalation terminated on 24 Nov	187	Lung slightly enlarged, but bloody color. No change in elasticity and luster. Several parts of lung surface congested and bloody. Speckles of miliary or rice size with slight hardness	Although lung system was healthy, partial congestion and hemorrhage. This change was obviously below the pleura where the pulmonary vesicle wall was condensated. Image of bronchitis in the lobus inferior. The dust cells gathered mostly in this portion filling the lymphatic tissue. Collapse of dust cells were not observed. Except for an image which showed a partial collapse of pulmonary vesicle, no change of other tissues and cells. Very few free dust particles
11	20 May to 13 Dec 41 (207 days) Inhalation terminated on 24 Nov	157	Almost the same as in the case of rabbit No. 9	Lacking any dust lung changes in the lung tissues, a partial collapse of the pulmonary vesicle wall. Some portions presented emphysema of the lung. Enlargement of lymphatic vessel and lymphatic glands. Other changes similar to rabbit No. 9

TABLE VI PATHOLOGICAL AND ANATOMICAL CHANGES IN THE LUNGS OF RABBITS WHICH INHALED CEMENT DUST

Rabbit Number	Experiment Period and Duration	Duration of Dust Inhalation, Hrs	Pathological and Anatomical Changes	
			Macroscopical Observations	Microscopical Observations
1	30 Jan to 30 Mar 51 (60 days)	50	Lungs dark brown with slight hardness and enlarged in size. Many pinhead sized cement colored minute speckles both below pleura and on crevices	Many dust particles gathered around blood vessels, lymphatic vessel, and bronchus where engorgement by dust cells were taking place. Dust cells and dust particles were entering blood vessels No isolated dust particles or collapsed cells in the tissues. Condensation and bleeding. Some portions showed emphysema of lungs. Obesity in lymphatic tissue and accumulation of dust particles and dust cells
5	31 Mar 41 to 2 Jul 42 (459 days) Inhalation terminated 24 Nov 41 to 15 Jan 42	345	Lungs hard and enlarged to remarkable size. Blue brown color. Cement colored minute speckles and dark colored miliary sized speckles on surface of lungs and crevices. Lymphatic gland in pulmonary hilus enlarged to bean size and conspicuous emphysema of the lung in both apeses. Slight emphysema of the lung in each lobe.	Transudation of liquid in pulmonary vesicle followed by condensation of lung. A portion of the dust particles isolated in the pulmonary vesicle walls, cell walls, and cell spaces. Dust cells appeared in large numbers. Many dust colonies below the pleura and showed obesity of lymphatic tissues. No collapse of dust cells and lung tissues. Congestion in the pulmonary vesicle wall was

			Lung was adhered to the diaphragm.	clearly observed and hemorrhage occurred at several points
8	15 Apr to 5 May 41 (21 days)	16	Lungs blood colored and soft. Hemorrhage and congested speckles. Abcut 15 cc. of transudated liquid below the pleural cavity	Larger portion of lung healthy, but some portions congested and blcd. Alveolar septa condensated. Aggregation of dust particles and dust cells in such section in large quantities. Many dust cells entered blood vessels. Transudated liquid in alveolar septa contained many dust particles. No emphysema of the lung and change of the lung tissue was generally slight
10	20 May 41 to 14 Feb 42 (271 days) Inhalation suspended from 24 Nov 41	185	Lungs hard, enlarged in size, and lacked elasticity. Many cement colored minute speckles, some larger than others. Lymphatic gland of pulmonary hilus remarkably enlarged to the size of bean. Emphysema in the apex of lung to a marked degree, especially, the superior lobe in right apex was 50% affected. No adhesion of the lung to the diaphragm.	Wall of the alveolar septa considerably congested. Appearance of dust cell observed to a marked degree, but only few dust particles were isolated in the tissue. Dust cells massed densely around blood vessel, lymphatic vessel, and bronchus. Such change clearly observed below pleura accompanied by obesity of the lymphatic tissue, and also presented an image of a partial dust lung colony. No collapse of the dust cells.

[illegible] VII PATHOLOGICAL AND ANATOMICAL CHANGES IN THE LUNGS OF RABBITS WHICH INHALED SILICON DIOXIDE

Rabbit [illegible]	Experiment Period and Duration	Duration of Dust Inhalation, hrs	Pathological and Anatomical Changes: Macroscopical Observations	Microscopical Observations
2	10 Feb to 21 May 41 (101 days)	84	Lungs dark-brown colored and enlarged in size remarkably. but lacked luster and elasticity. Many dark minute speckles on faces and crevices of superior lobe and around pulmonary hilus. Congestion and blood speckles below pleura. Conspicuous emphysema of lung in both pulmonary apexes and inferior lobe.	Images of condensated wall of the pulmonary hilus. Many dust cells and dust particles in every part aggregated in blood vessels, lymphatic vessels, and bronchus. Enlargement of pulmonary hilus, but not distinct due to intrusion of mucous like substance. Collapse of dust cells. Lymphatic tissues, enlarged and filled with dust cells and dust particles. Homorrhage occurred only slightly. No occulusion of the blood vessel or silicotic lung.
7	15 Apr to 21 May 41 (37 days)	31	Lungs had comparatively good luster with elasticity. Black minute speckles below pleura outside lung and in pulmonary hilus. No hemorrhage or congestion.	Lung tissue generally healthy. Portion of pulmonary hilus wall enlarged and many dust cells appeared. No transudated substance of lung cells or emphysema of lung. Many dust cells mingled into the blood vessel. No hemorrhage collapse of pulmonary hilus wall.

Incl 17, Report TID, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dtd 15 Dec 48

12	22 May to 30 May 41 (9 days)	8	Very few hemorrhages and congested speckles in right lung and in inferior lobe. The lung lacked luster and slightly colored dark-brown.	Large number of dust particles isolated in intermediate substance. Some dust cells in the state of collapse. Other points same as rabbit No. 7
13	22 May 41 to 18 Jun 42 (393 days) Inhalation suspended between 24 Nov 41 and 15 Jan 42	289	Lungs harden and considerably enlarged in size, lacked luster and colored greyish-brown. Very many minute black speckles in both lungs. Pin-head and miliary sized black speckles in upper regions, which were arranged in radial pattern from pulmonary hilus Emphysema of lung clearly observed on upper regions of both lungs, which extended to 50% of inferior lobes. Medium degree of emphysema of lungs on lower and anterior regions. The lower apex of right lung adhered to diaphragm.	Collapse, obesity, and hemorrhage of pulmonary hilus. Many pulmonary hilus showed symptoms of emphysema of lungs. Many dust cells and dust particles in lungs, a portion showed image of collapse. Connective tissue cells were mingled. Dust colonies clearly observed below pleura and some occluded blood vessels. Obesity of lymphatic tissues seen in marked degree and lymphatic vessels enlarged. Free dust particles found isolated in tissue. Collapse of every type of cells. Degree of condensation became greater characterized by thickening of connective tissue. Recognized commencement of silicotic lung.
14	31 May to 8 Jun 41 (9 days)	8	Similar to rabbit No. 12.	Similar to rabbit No. 12.
15	28 Jul to 10 Aug 41 (13 days)		"	"
18	8 Aug to 13 Aug 41 (5 days)		"	"

RESEARCH CONCERNING INHALATION OF MICROSCOPIC FOREIGN SUBSTANCES

Part I - EXPERIMENT ON INHALATION OF MICROSCOPIC FOREIGN SUBSTANCES BY HEALTHY ANIMALS

by

Kiyoyoshi HORIGUCHI, Department of Surgery, Faculty of Medicine, Osaka University

(published in J. Osaka Med. Assn. (Japan), 35, 365 (1936)

A. SUMMARY:

In order to determine in which pulmonary region a greater amount of inhaled foreign substances (such as soot dust, carmine pigment powder, and zinc oxide powder) settles, the dust deposited in the upper and lower pulmonary regions were examined and compared. The inhaled soot dust was macroscopically inspected, while the carmine deposit was colorimetrically determined, and the amount of zinc oxide was quantitatively analyzed. These examinations proved that the upper lobe of the lung contained a greater amount of inhaled dust particles than the regions below it and that the right lung has a somewhat larger deposition than the left lung. From this fact it was concluded that the upper lobe was more active in the respiratory action than the other regions.

B. INTRODUCTION:

An animal body has various organs by means of which the inhaled dust particles can be expelled, the most important of which is the filtration action in the upper regions of the respiratory tract by the ciliary motion of the epithelial cells. The inhaled dust particles, adhering to the mucous membrane, can be dislodged by sneezing or coughing and those wrapped in the mucus are expectorated or swallowed. The dust particles which have reached the deeper bronchial branching, where the expectorating force by coughing is weak, are driven out chiefly by the ciliary motion. If the dust particles penetrate any deeper, it enters the alveoli where, although a portion of the dust particles are driven out of the body by means of exhalation, greater portion is settled. A portion of the dust particles settling in the alveoli is consumed by the cells to be eliminated from the body, and the remainder of the dust particles penetrate the pulmonary tissue. The dust particles which have penetrated the pulmonary tissue are carried through the pulmonary lymphatic vessel to settle among the tissues under the pleura or in the bronchial lymphatic glands. Through such mechanisms and functions as explained above, animal lungs continuously perform the

auto-cleansing function. However, the distribution of the dust particles in the various pulmonary regions and the cleansing effect in these regions do not appear to be uniform.

In this experiment the animals were made to inhale soot dust, carmine pigment powder, and zinc oxide powder in order to examine the settlement of microscopic foreign particles in their lungs, the difference between the amount of deposition in the left and the right lungs, and also the amount of deposition between the upper and the lower lobes of the lungs.

C. TEST ANIMALS AND METHOD:

The microscopic foreign substances, soot dust, carmine pigment powder, and zinc oxide powder, were inhaled over a period of time by the test animals, rabbits, goats, and dogs.

1. Method of Inhalation: The animals were made to inhale soot dust which was prepared by burning a kerosene lamp, allowed to pass through a 3 m flue, and circulated in a well ventilated box 1 meter cube. Carmine powder was blown by pressure into a narcotizing box containing the test animals. The zinc oxide powder was stirred up in the air and introduced through the top of the narcotizing box. It was necessary that care must be taken in order to see that the test animals are resting in their natural pose without exerting undue pressure on their thorax.

2. Detection and Comparison of Inhaled Dust Deposit: The animals which inhaled the dust particles for a definite period were killed and their tracheae were ligatured at the neck to prevent the escape of the air inhaled into the lungs. The lungs were opened and the deposition of the foreign substances were macroscopically and histologically inspected. The left and right lungs, as well as the upper and lower regions of the lung, were compared as to the amount of dust deposition. Histological specimens were made of the pulmonary hilus lymphatic gland and such internal organs as the spleen, liver, kidney, and the lymphatic gland on the anterior wall of the abdominal cavity in order to examine the settlement and transition of foreign substances into these regions from the lungs. The inhaled soot dust was macroscopically inspected; carmine powder deposit was colorimetrically determined; and the zinc oxide was quantitatively analyzed for zinc.

D. RESULTS OF EXPERIMENT:

1. Macroscopical and histological observation of the respiratory organs and rarely showed inflammatory changes. The results of the experiment are tabulated in Table I.

TABLE I - SOOT DUST AND CARMINE POWDER INHALATION TEST

Test	Animal and Serial Number	Inhalation Period, days	Inhalation Period, per day	Interval between Last Inhalation and Death	Amount of Soot Dust Deposition			
					Left Lung		Right Lung	
					Upper Lobe	Lower Lobe	Upper Lobe	Lower Lobe
Soot Dust	Rabbit							
	96	1	10 min.	30 min.	xx	x	xx	x
	104	6	10 hr.	immediately	x	x	x	x
	101	10	8 hr.	immediately	x	x	x	x
	105	4	12 hr.	10 days	xx	x	xx	x
Carmine Powder	Rabbit				Amount of the carmine powder deposit could not be made due to similarity of the carmine color and the lung tissues.			
	1	1	3 hr.	immediately				
	2	1	3 hr.	3 hr.				
	3	1	3 hr.	6 hr.				
	8	1	3 hr.	15 hr.				
	9	1	3 hr.	21 hr.				
	4	1	3 hr.	24 hr.				
	12	1	3 hr.	3 day				
	10	1	3 hr.	4 day				
	Dog							
	58	5	20 min.	7 day				
	26	16	30 min.	14 day				

NOTE: (xx) denotes pronounced soot dust deposition and (x) slight deposition

Neither macroscopic observation nor histological examination detected any difference between the deposition of soot dust and carmine powder in the lungs. The amount deposited in the left and right lungs as well as upper and lower lobes were about equal, although it was found that a slightly greater amount was found deposited in the upper lobe than the lower lobe. When rabbits inhaled soot dust for a long period, the soot dust particles concentrated in the Acini and its surface and crevices appeared like a leopard skin under macroscopical inspection. When carmine powder was continuously inhaled for three hours, its presence could not be distinguished with the naked eye, partially because of the color being the same as the lung and partially because there was so little deposited amount. The microscopic foreign substances, which had been inhaled and deposited in the lungs, were eaten by the cells and the soot dust cells began to appear 40 minutes after the beginning of inhalation. Carmine cells also must have appeared in the early stage of the inhalation because a large number were detected three hours after the first inhalation. Nearly all the free dust particles (soot dust and carmine powder) disappeared in the rabbits and dogs three days after the last inhalation. The few free dust particles

were observed to be chiefly concentrated in the alveolar tract, small bronchioli respiratorii space, and the neighboring alveolar space. The development of the dust cells were most pronounced in the interior of the bronchial branchings. Most of the microscopic foreign substances in the respiratory duct were expectorated either in the free state or after being eaten by the cells. Therefore, after the inhalation of the microscopic foreign substances ceased, the amount of foreign dust particles in the respiratory duct gradually decreased with the elapse of time.

The deposition of soot dust cells could be perceived 40 minutes after the commencement of inhalation, although the amount was very small, in the lymphatisch gewebe of the Acini and in the pulmonary lymphatic glands existing immediately under the mucous membrane of the trachea. The inhaled foreign substances reached the lymphatic gland of the pulmonary hilus six hours after the commencement of inhalation (Rabbit No. 6). As the time elapsed, the amount of foreign substance in the lungs and pulmonary lymphatic glands gradually increased and were found deposited in either the medullary or the cortical portion. Although the amount of foreign substances deposited in the lymphatisch gewebe was very small compared with that in the lungs during the early stages of inhalation, the retention of the foreign substance in the lymphatisch gewebe was long.

It was very difficult to macroscopically and histologically compare the amount of microscopic foreign substances deposited in the left and right pulmonary lymphatic glands due to their position and connection with the lymphatic vessels. The lymphatic glands in the abdominal cavity and the anterior abdominal wall of the dog and the entrails, such as the liver, spleen, and kidneys of rabbits and dogs, were inspected and it was found that the carmine pigment or soot dust particles did not exist in spite of the prolonged inhalation.

2. For the purpose of accurate comparison of the left and the right lung as to the deposited amount of carmine pigment, the carmine colorimetry test was performed and it was found that the amount of carmine pigment deposit, capable of colorimetric detection, was comparatively large. The colorimetry test was carried out with samples from each pulmonary lobe, but the method was unsatisfactory, unless the amount of carmine pigment inhaled was sufficiently large, due to the fact that the color of the tissue when transferred to the ammonia solution obscures the carmine color. Therefore, the results of this colorimetric test can not be relied upon, but the method is far superior to the macroscopic or histologic method for comparing the amount of carmine pigment deposited in the left and right lungs.

The results are tabulated in Table II.

TABLE II - CARMINE INHALATION TEST

Animal and Animal Number	Inhalation Period, days	Inhalation Time per Day, hours	Interval Between Last Inhalation and Death	Ratio of Carmine Deposit	
				Right Lung	Left Lung
Rabbit					
70	1	4	2 days	1.0	1.0
72	2	3	1 day	1.0	0.9
84	4	3	immediately	1.0	1.1
85	4	3	4 days	1.0	1.1

As shown in Table II, the ratio of the carmine deposit between the left and the right lungs is 1.0:1 0 with a deviation of approximately 0.1 regardless of the time which elapsed after the inhalation.

3. Zinc oxide: In order to make sure that the quantitative analysis of zinc oxide was suitable for the purpose of this experiment, a preliminary test was performed, and the results, as shown in Table III, were obtained: i.e. when an ashless filter paper is used, 94.2% of the added zinc can be determined by quantitative analysis; when 1 g sample of dehydrated lung tissue unexposed to zinc oxide was tested, no zinc could be detected; but when zinc was added, 90.5% to 93% of the added zinc can be recovered. Thus, this preliminary test proved that the quantitative determination for zinc was satisfactory.

TABLE III

Sample	Zinc oxide added (mg)	Zinc oxide determined	
		(mg)	(% recovery)
Ashless filter paper, 1 sheet	1.00	0.93	93.0
"	2.00	1.91	95.5
Dehydrated lung tissue, 1 g	0	0	0
(unexposed to zinc 1 g	1.00	0.93	93.0
oxide dust) 1 g	2.00	1.81	90.5

Macroscopical and histological inspection of the respiratory system of dogs and goats disclosed no inflammations when the animals were made to inhale zinc oxide dust. However, immediately after the inhalation, a secretion containing zinc oxide was noted in the trachea and bronchial cavity. A large quantity of zinc oxide deposit was found in the interior

of the bronchial branchings. Most of the zinc oxide in this cavity disappeared [illegible] hours after the inhalation. The results obtained were the same as in the case of the carmine pigment inhalation. However, the zinc oxide, which settled in the Acini was very fine and white, was very difficult to detect either macroscopically or histologically.

Table IV shows the result of the comparison of the amount of zinc oxide deposited between the upper and lower regions of the lung and also between the left and right lungs. In the case of the goats, the amount of zinc oxide deposited was greater in the right lung than in the left lung, the former being in the ratio of 1.0 to 0.9-1.0 to the latter. Also the upper lobe contained a slightly larger amount of zinc oxide deposit than the lower, the ratio of the deposited amount between the right upper lobes and the right central, lower, and mediastinum lobes (or between the left upper lobe and the left lower lobe which included the left central lobe) was 1.0: 0.8-0.9. In the case of the dogs, the ratio was approximately the same as in the case of the goats.

TABLE IV - ZINC OXIDE INHALATION EXPERIMENT

Animal and Animal Number	Inhalation Period	Interval Between Last Inhalation and Death	Ratio of the Deposited Amount (mg %)			
			Right Upper Lobe / Right Central, lower, & Mediastinum Lobes	Left Upper Lobe / Left Lower Lobe	Upper Lobes / All Other Lobes	Right Lung / Left Lung
Dog 1	1 hour	30 mins.	1.0/1.0	1.0/0.7	1.0/0.9	1.0/0.8
2	1 hour	30 mins.	1.0/0.7	1.0/1.0	1.0/0.9	1.0/1.0
3	1 hour	30 mins.	1.0/1.0	1.0/0.9	1.0/1.0	1.0/0.9
Average for dogs			1.0/0.9	1.0/0.9	1.0/0.9	1.0/0.9
Goat 24	10 mins.	immediately	1.0/1.1	1.0/1.1	1.0/1.1	1.0/0.9
27	10 mins.	immediately	1.0/1.0	1.0/0.8	1.0/1.0	1.0/0.9
9	2 hours	immediately	1.0/0.9	1.0/0.7	1.0/0.8	1.0/0.9
3	1 hour	28 hours	1.0/0.8	1.0/0.9	1.0/0.8	1.0/0.9
14	4 days (70 mins. per day	30 mins.	1.0/0.9	1.0/0.9	1.0/0.9	1.0/1.0
10	2 hours	3 days	1.0/0.9	1.0/0.9	1.0/0.9	1.0/0.9
Average for goats			1.0/0.9	1.0/0.9	1.0/0.9	1.0/0.9

E. DISCUSSION AND CONCLUSION:

The author summarizes the results of the experiments and concludes that the greatest amount of dust deposition occurs when (1) a large amount of dust is inhaled, (2) the expectorated amount of dust particles is small compared to the amount inhaled, and (3) a small amount of the dust particles deposited in the system is removed through the lymphatic glands. These conditions are greatly influenced by the respiratory movement of the pulmonary vesicles.

In this experiment, it was found that the foreign substances, soot dust, carmine pigment, and zinc oxide powder, were found to settle in the right lung in greater amount than the left lung, and the upper lobes deposited a greater amount than the lower lobes.

RESEARCH CONCERNING INHALATION OF
MICROSCOPIC FOREIGN SUBSTANCES
Part II EXPERIMENT OF LUNGS ATROPHIED PRIOR
TO INHALATION OF MICROSCOPIC FOREIGN SUBSTANCES

by

Dr. Kiyoyoshi HORIGUCHI, Department of Hygiene,
Faculty of Medicine, Osaka University, Osaka

(Published in J. Osaka Med. Assn. (Japan), 35, 547-551 (1936)

A. SUMMARY:

A test animal, whose lung had been atrophied by such treatment as pneumothorax, phrenicectomy, and thoracoplasty, was made to inhale microscopic foreign substances. Both lungs were examined upon completion of the experiments by methods mentioned in Part I for the settlement of inhaled foreign substances. Through this examination it became known that in those pulmonary regions where the respiratory function had been diminished by the above-mentioned atrophy a comparatively small amount of inhaled foreign substances settled.

B. INTRODUCTION:

In Part I, the author reported as a conclusion of the dust inhalation experiment with healthy test animals that the inhaled foreign substances settled in the right lung in a greater degree than in the left, and that the upper lober contained a greater amount of dust deposition than the other regions below it.

In this experiment, the lung of the test animal was atrophied prior to the inhalation of dust through such treatment as pneumothorax, phrenicectomy, and thoracoplasty to determine the influence of such treatments upon the settlement of inhaled foreign substances in the lung.

In 1907, UNIMIYA, while studying under Dr. BRAUER, observed that very little of the inhaled coal dust particles settled in the atrophied lung. KUWA, who had performed a similar experiment, reported that in the case of the rabbits, the atrophy pronouncedly reduced the soot dust deposition, but the influence of atrophy on dust inhalation was not very appreciable in the case of dogs. KUWA explained that the difference between the dogs and rabbits are due to the difference in toughness of their mediastina and to the variation in the function of their thoraxes in regulating the respiratory motion.

C. METHOD OF EXPERIMENT

Adult rabbits, each weighing 2-2.5 kg and goats, each weighing 6-10 kg were used as test animals. After one of the two lungs was atrophied, a test animal was made to inhale microscopic foreign substances, such as soot dust, carmine pigment powder, and zinc oxide powder. The test animals were killed after lapse of fixed period of dust inhalation. Both lungs were extracted, immediately after their death, to examine the difference between the atrophied and normal lung with respect to the amount of inhaled microscopic foreign substances.

Methods used to make the test animals inhale the microscopic foreign substances and the method of comparison of the upper and lower lobes and the left and right lungs were conducted as mentioned in Part I. Pneumothorax, phrenicectomy, or thoracoplasty was performed on the test animals as follows:

1. Pneumothorax: The test animal's body was fastened so that it could not move and the pneumothorax operation was performed under sterilized conditions. At first 30 cc/kg body weight of air was administered. In the case of rabbits, air was admitted and changed at intervals of 6 days with the admittance of 30-40 cc of air at one time.

2. Phrenicectomy: The 4th and 5th cervical nerves were closely examined to locate the phrenic nerve which was followed up to the angulus venosus where the phrenic nerve was pinched and extracted. Since the big nerve root, starting from the 5th cervical nerve of the goat, lies deeply buried among the musculus obliquo, the extraction of the phrenic nerve was carefully performed without harming the other nerves.

3. Thoracoplasty: Thoracoplasty was performed according to TAKEDA's method. The synchrondrosis after the costotomy was unsuccessful in the case of goats due to the cartilagine property of the costa and the respiratory movement. Therefore, the costa only was cut and 3 to 4 cm of both ends were folded with one upon the other and tightly bound with aluminum bronze wire.

D. RESULTS OF THE EXPERIMENT

1. Soot Dust Inhalation Test: The over-all results, of the soot dust inhalation experiment are shown in Table I. According to the macroscopic and histologic examination, the atrophied lung contained definitely smaller amounts of soot dust deposition than the other normal lung. Although the upper lobe of both lungs, atrophied and normal, and a greater amount of soot dust deposition compared with its lower lobes, the actual deposited amount of dust particles was less in the atrophied lung and the degree of reduction varied with the method of atrophy.

Incl 13, Report TIS, GHQ, FEC, APO 500, subject: "Locus of Impaction of Particulates," dated 15 Dec 48

In the case of artificial pneumothorax, the deposited amount of soot dust particles in the atrophied lung was evenly reduced regardless of the region. The ratio of the deposited amount of soot dust particles between the upper and the lower lobes was the same as in the case of healthy animals. In the case of phrenicectomy, the difference in the deposition between the upper and lower lobes of the atrophied lung became appreciably marked, with the upper lobe containing a much greater amount of deposition. In the case of thoracoplasty, the breast wall was vertically upheaved into the thoracal cavity at a region about 1 to 2 cm apart from the back bone. With the upper and the lower lobes immediately behind the upheaval being directly pressed, the pulmonary regions thus pressed became evacuated and contracted. Consequently, the dust deposition could not be perceived in this particularly atrophied region, whereas the deposition was noticeable in the central lobe which was not directly pressed.

TABLE I - DEPOSITION OF SOOT DUST PARTICLES IN THE ATROPHIED AND NORMAL LUNGS OF RABBITS

Method of Atrophy and Rabbit Number	Duration of Inhalation, days	Inhalation Period per Day, hrs.	Interval between Atrophy and Death, days	Interval between Last Inhalation and Death, days	Comparison of Soot Dust Deposition			
					Atrophied Lung	Normal Lung	Atrophied Upper Lobe / Lower Lobe	Normal Upper Lobe / Lower Lobe
Pneumothorax					(x)		(x)	
109	10	14	10	same day	-	*	-/-	-/-
97	3	8	11	6	-	*	*/-	*/-
98	7	14	18	2	-	-	*/-	*/-
Phrenicectomy								
120	3	14	4	1	-	*	*/-	*/-
124	2	8	10	1	-	*	*/-	*/-
125	4	8	20	2	-	*	*/-	*/-
Thoracoplasty								
650	3	14	9	same day	-	*	-/-	*/-
651	4	8	15	1	-	*	*/-	*/-
652	4	8	21	1	-	*	*/-	*/-

NOTE: * denotes pronounced soot dust deposition
- denotes slight soot dust deposition
(x) Right lung was atrophied in every case

Regardless of the atrophy method, the deposited amount of soot dust particles in the mediastinum lobe of the atrophied lung was nearly equal to that in the same region of the healthy lung. The atrophy caused no histological changes in the atrophied lung, but reduced the deposited amount of inhaled dust particles.

2. Carmine Pigment Inhalation Test: The carmine pigment inhalation test was performed on rabbits whose lungs had been previously atrophied. The amount of deposited carmine pigment was determined by the colorimetry test and the results are tabulated in Table II.

TABLE II - DEPOSITION OF CARMINE PIGMENT IN THE ATROPHIED AND NORMAL LUNGS OF RABBITS

Method of Atrophy and Rabbit Number	Duration of Inhalation, days	Inhalation Period per Day, hrs.	Interval between Atrophy and Death, days	Interval between Last Inhalation and Death, days	Atrophied Lung	Ratio of Carmine Pigment Deposit: Atrophied Lung	Ratio of Carmine Pigment Deposit: Normal Lung
Pneumothorax							
75	1	3	same day	same day	left	0.3	1.0
761	3	1	5	2	right	0.8	1.0
Phrenicectomy							
312	3	0.5	11	3	right	0.6	1.0
313	3	0.5	22	6	right	0.4	1.0
86	1	1	45	same day	left	0.6	1.0
Thoracoplasty							
76	2	3	2	same day	left	0.9	1.0
364	3	0.5	10	same day	right	0.9	1.0
87	1	3	38	same day	left	0.7	1.0

In the case of pneumothorax, the reduction of the carmine deposit in the atrophied lung is very pronounced when the carmine pigment inhalation was made immediately following the atrophy. When the inhalation is commenced some time after the atrophy and the animal killed after lapse of several days, the deposition of carmine pigment in the atrophied lung was not so marked. In the case of phrenicectomy, the carmine deposit in

the atrophied lung was small compared to that in the normal lung. Unlike the case of pneumothorax, the time interval from the atrophy to death or from the last inhalation of carmine pigment to death appeared to have little influence upon the amount of deposition. The deposit of carmine pigment in the atrophied lung was from 40 to 60% of that of the normal healthy lung. In order to determine the difference in the deposited amount among the various pulmonary lobes, the lungs of the rabbit No. 813 was divided into three parts; i.e. the first part consisting the right upper, central and lower lobes, the second part consisting of the mediastinum lobe, and the third part consisting of the left upper and lower lobes. The ratio of the deposited amount of carmine pigment among these three parts was 1.0 : 1.8 : 2.6/ Through this ratio a comparatively small deposit was contained in the right lung which was atrophied, but the mediastinum lobe contained a larger amount in comparison with the other pulmonary regions of the right lung. The reason for this is considered to be as follows: Although the mediastinum lobe belongs to the right lung, anatomically a portion of the mediastinum lobe projects into the left pleural cavity so deeply that even after the right diaphragm has stopped moving, the spatinum mediastinale is able to continue its respiratory action by movement of the left diaphragm. In the case of rabbit No. 86, the left lung was subjected to phrenicectomy and as a consequence the carmine dust deposition in the atrophied lung decreased to 40% of that of the normal lung. From these experimental facts, it can be concluded that the influence of phrenicectomy upon the deposition of dust particles is nearly equal in the left and the right lungs and if any difference does exist, the difference is due to the position of the spatinum mediastinale.

In the case of TAKEDA's method of thoracoplasty, the atrophied organs also decreased in the amount of carmine pigment deposit. The influence of thoracoplasty upon the deposition of carmine pigment varied with the degree of costal contraction. When the right lung of rabbit No. 864 was atrophied through thoracoplasty, the ratio of carmine pigment deposition in the various lobes was as follows: right upper lobe, 1.1 : right central lobe, 1.5 : right lower lobe, 1.0 : spatinum mediastinale, 1.5 : left upper lobe, 1.1 : and left lower lobe, 1.2. In the case of the thoracoplasty, the pulmonary region where the costa is especially shortened, i.e. the rear region of the lung, was markedly atrophied while the frontal pulmonary region, especially the central and the spatinum mediastinale lobes, became emphysematous with increased alveoli pulmonum.

3. Zinc Oxide Inhalation Test: The results of the experiment on goats which inhaled zinc oxide dust after the lungs were atrophied are tabulated in Table III.

TABLE III - DEPOSITION OF ZINC OXIDE DUST IN THE ATROPHIED AND NORMAL LUNGS OF GOATS

Method of Atrophy and Goat Number	Duration of Inhalation, days	Inhalation Period per Day, hrs.	Interval between Atrophy and Death, days	Interval between Last Inhalation and Death, days	Ratio of Zinc Oxide Deposit			
					Atrophied Lung	Normal Lung	Atrophied Upper Lobe / Lower Lobe	Normal Upper Lobe / Lower Lobe
Pneumothorax 13	1	1	same day	same day	0.4	1.0	1.0/0.9	1.0/1.0
Phrenicectomy 5	2	1	9	3	0.7	1.0	1.0/1.5	1.0/1.0
Thoracoplasty 20	1	1	same day	same day	0.8	1.0	1.0/0.9	1.0/0.8

Table III indicates that the amount of zinc oxide deposited in the atrophied lung is small compared to that of the normal lung on the opposite side, the former being 40% of the latter in the case of pneumothorax, 70% in the case of phrenicectomy, and 80% in the case of thoracoplasty. In general, the upper lobe contained a larger amount of deposition than the regions below it. Except in the case of phrenicectomy the lower lobe contained more than the upper lobe due to the position of the spatinum mediastinale.

E. SUMMARIZATION AND DISCUSSION:

Lung atrophy aims at the relaxation or repose of the lung. This relaxation or repose accompanies the reduction in the volume of air inhaled into or exhaled out of the alveoli. It is reasonably presumed that this change in the volume of air in the respiratory system must produce some influence upon the settlement of inhaled foreign microscopic particles. It is very interesting to re-examine the results of this experiment by taking this view point into consideration.

It is apparent from the results of the researches conducted by many medical men with X-rays that the pneumothorax fills the pleural cavity with air and presses the lung toward the pulmonary hilus. In the soot dust and carmine pigment inhalation test, the experiment proved that pneumothorax greatly diminished the dust deposition in the atrophied lung in

comparison with the healthy lung. Macroscopic observations revealed that the upper lobe of the atrophied lung contained a larger amount of dust deposition than its lower lobes. The carmine colorimetry test also confirmed this fact; and it was ascertained that the ratio of the deposit between the upper and lower lobes of the lung atrophied through pneumothorax was the same as that of the healthy lung. This coincides with the conclusions obtained through clinical study; i.e. the pneumothorax presses the pulmonary tissue towards the pulmonary hilus. When the period between the performance of pneumothorax and the inhalation of foreign microscopical substances is long, there is less appreciable reduction of dust deposition in the atrophied lung. This also corresponds to the clinically and experimentally proved facts that the air stored in the pleural cavity through pneumothorax is gradually absorbed, with the atrophied lung recovering its normal and healthy condition. Thus, through this observation, it can be stated that the deposited amount of inhaled foreign microscopical substances is proportional to the alveolar expansion or contraction of the lungs.

There was no notable relationship observed between the reduction of the dust deposition caused by phrenicectomy and the time interval from the atrophy to death or from the last inhalation of dust particles to death. This indicates that the lung is atrophied immediately upon the performance of phrenicectomy and the atrophied lung can not recover its normal condition. When phrenicectomy was performed, the lower lobe was most effectively atrophied, whereas the spatinum mediastinale lobe was only slightly influenced due to its anatomical structure.

In the case of thoracoplasty, the atrophy reduced the dust deposition only to a slight degree.

F. CONCLUSIONS:

When the lungs of healthy goats and rabbits were atrophied, the settlement of the inhaled microscopical foreign substance was influenced as follows: The pulmonary region where the respiratory function was impeded to the greatest degree contained a small amount of dust deposition; while the regions, whose respiratory action was only slightly weakened, possessed a comparatively large amount of dust deposition. In the case of pneumothorax, although the actual amount deposited in the atrophied lung was reduced, the ratio of the dust deposition among the various pulmonary regions of the atrophied lung was the same as that of the other normal lung. In the case of phrenicectomy, the central and the lower lobes contained the smallest amount of dust deposition. In the case of thoracoplasty, the effect of atrophy was not appreciable.

RESEARCH CONCERNING INHALATION OF MICROSCOPIC FOREIGN SUBSTANCES
Part III EXPERIMENT OF LUNGS ATROPHIED AFTER INHALATION OF MICROSCOPIC FOREIGN SUBSTANCES

by

Dr. Kiyoshi HORIGUCHI, Department of Hygiene,
Faculty of Medicine, Osaka University, Osaka

(published in J. Osaka Med. Assn. (Japan), 35, 663-668 (1936))

A. SUMMARY

When a lung of an animal was atrophied after inhalation of microscopic foreign substances, the pulmonary region, whose respiratory function was curtailed due to the atrophy, contained a large amount of inhaled foreign substances.

B. INTRODUCTION

The author reported the experiment regarding the inhalation of microscopic foreign substances by healthy animals in Part I and the experiment regarding the inhalation of foreign substances by animals after their lungs have been atrophied.

In this experiment, one of the lungs of the animal, which had already inhaled the microscopic foreign substances, was atrophied through either pneumothorax, phrenicectomy, or thoracoplasty to examine the settlement of the inhaled microscopic foreign substances into the atrophied lung.

C. METHOD OF EXPERIMENT

Rabbits, each weighing 2-3 kg, and goats, each weighing 7-16 kg, were used as the test animals.

After the animals inhaled microscopic foreign substances, such as: soot dust, carmine pigment, and zinc oxide, one of its two lungs was atrophied. Then, after elapse of definite period of time, the animal was killed to determine the amount of the foreign substances deposited in each lung.

The method used to make the animal inhale foreign substances and the method for comparing the deposited amount of foreign substances were the same as in the experiment with healthy animals as explained in Part I.

D. RESULT OF EXPERIMENT

1. Coal Dust Inhalation Test: The results of the experiment in which a lung of the test animals was atrophied after inhalation of soot dust particles are given in Table I.

TABLE I - DEPOSITION OF COAL DUST IN THE LUNGS OF RABBITS FOLLOWED BY ATROPHY

Method of Atrophy and Animal Number	Inhalation Period, days	Inhalation Time per Day, hours	Atrophied Lung	Interval from Atrophy to Death	Interval between First Inhalation to Death, days	Comparison of Soot Dust Deposition			
						Atrophied Lung	Normal Lung	Atrophied Upper Lobe / Lower Lobe	Normal Upper Lobe / Lower Lobe
Pneumothorax									
102	6	10	right	30 mins.	6	*	-	-/-	-/-
108	7	10	right	2 days	8	*	-	*/-	*/-
103	4	15	right	7 days	10	*	-	-/-	*/-
109	3	14	left	13 days	15	*	-	-/-	-/-
99	3	14	right	30 days	32	*	-	*/-	-/-
Phrenicectomy									
111	4	8	right	3 days	6	*	-	-/*	-/-
112	4	8	right	3 days	6	*	-	-/*	-/-
113	4	7	right	6 days	9	*	-	-/*	-/-
602	4	6	right	14 days	17	-	-	-/*	*/-
Thoracoplasty									
551	3	16	right	6 days	6	*	-	*/-	-/-
552	3	16	right	10 days	12	*	-	*/-	*/-
553	4	15	right	23 days	26	*	-	*/-	*/-

NOTE: * denotes pronounced soot dust deposition
- denotes slight deposition

The deposition of soot dust particles in the atrophied lung by either pneumothorax, phrenicectomy, or thoracoplasty was greater when compared with that in the normal lung. This is due to the fact that the atrophy reduced the air volume in the respiratory system and impeded the expectoration of the inhaled dust particles. The degree of deposition of dust particles.

... degree of deposition of dust particles in the various pulmonary regions varied with the method of atrophy.

In the case of pneumothorax, the upper lobe contained a greater amount of soot dust deposition than the other regions. Pneumothorax atrophies the lung towards the pulmonary hilus and contracted the pulmonary region equally; thus the ratio of the deposition amount the various regions of the atrophied lung was the same as the healthy animals. In the case of phrenicectomy, the settlement of foreign substance was especially noticeable in the lower lobe when compared with the upper lobe where the deposition of foreign substances was undistinctive. This is considered to be due to the fact that phrenicectomy atrophies the lower lobe in the greatest degree and consequently the rate of expectoration of the foreign substances inhaled into the lower lobe is greatly delayed. In the case of thoracoplasty, soot dust deposition was comparatively pronounced in the upper lobe.

2. Carmine Pigment Inhalation Experiment: A lung of the test animal which had inhaled carmine pigment powder was atrophied and then the amount of carmine pigment deposited in both lungs was measured by means of the colorimetry test. The results of the experiment are tabulated in Table II.

TABLE II - DEPOSITION OF CARMINE PIGMENT IN THE LUNGS OF RABBITS FOLLOWED BY ATROPHY

Method of Atrophy and Rabbit Number	Inhalation Period, days	Inhalation Time per Day, hours	Atrophied Lung	Interval from Atrophy to Death, days	Interval from First Inhalation to Death, days	Ratio of Carmine Pigment Deposition	
						Atrophied Lung	Normal Lung
Pneumothorax							
34	1	3	left	2	2	1.0	0.8
39	1	5	left	4	4	1.0	0.9
751	2	1.5	right	5	6	1.0	0.8
Phrenicectomy							
13	1	2	left	2	2	1.0	0.7
32	5	0.5	left	3	7	1.0	0.9
301	3	1	right	5	7	1.0	1.0
Thoracoplasty							
74	2	1	left	5	6	1.0	1.0
19	3	0.5	right	11	13	1.0	0.5

Regardless of the method of atrophy, the atrophied lung contained a larger amount of deposition of carmine pigment than the normal lung. The results of this experiment coincides with the results of the soot dust inhalation test.

3. Zinc Oxide Inhalation Test: A lung of a test animal, which had inhaled zinc oxide powder, was atrophied and the amount of zinc oxide dust deposited in the lungs was measured. The results of the experiment are tabulated in Table III.

The atrophied lung of the goat contained a greater amount of zinc oxide deposition than the other normal lung. In the cases of pneumothorax and phrenicectomy, the difference in the amount deposited between the upper and lower lobes of the atrophied lung was similar to that ascertained in the author's experiment with healthy animals. However, in the case of thoraco-pasty, the lower lobe contained a larger amount of zinc oxide deposit.

TABLE III - DEPOSITION OF ZINC OXIDE DUST IN THE LUNGS OF GOATS FOLLOWED BY ATROPHY

Method of Atrophy and Goat Number	Inhalation Period, days	Inhalation Time per Day, hours	Atrophied Lung	Interval from Atrophy to Death, days	Interval from First Inhalation to Death, days	Ratio of the Zinc Oxide Deposition			
						Atrophied Lung	Normal Lung	Atrophied Upper Lobe / Lower Lobe	Normal Upper Lobe / Lower Lobe
Pneumothorax 15	1	2	left	2	2	1.0	0.8	1.0/0.8	1.0/1.0
Phrenicectomy 11	4	1	left	5	8	1.0	0.7	1.0/1.0	1.0/0.8
12	1	4	right	10	10	1.0	1.0	1.0/1.5	1.0/1.0
Thoracoplasty 7	1	2	right	2	2	1.0	1.0	1.0/1.0	1.0/1.0

V. INFLUENCE OF LUNG WEIGHT CHANGE CAUSED BY ATROPHY ON THE COMPARATIVE RATIO OF MICROSCOPIC FOREIGN SUBSTANCE DEPOSITION

Atrophy reduces the weight of the treated lung. The weight of the lung is an important factor in determining the amount of zinc oxide dust particles in the lung. Therefore, the fact that the atrophy changes in the weight of the treated lung must be taken into consideration in determining the amount of zinc oxide deposition. Lungs of 11 healthy goats were dessicated to determine the weight ratio between both lungs. The arithmetic mean value of the weight ratio between right and left lung was 1.39 : 1.00 with a maximum ratio of 1.55 : 1.00 and a minimum ratio of 1.30 : 1.00. In order to determine what changes the atrophy caused in the weight of the treated lung, the following experiment was carried out:

1. Pneumothorax: When the left lung of goat No. 18 was atrophied through pneumothorax, the weight ratio between its two lungs was 1.39 : 1.00. However, in the case of goat No. 15, which was left untouched for 2 days after the atrophy and then examined, the ratio was 1.34 : 1.00 which is approximately the same as arithmetic mean value.

2. Phrenicectomy: The right lungs of 5 goats were atrophied through phrenicectomy to determine the weight ratio between their left and right lungs whose arithmetic mean value was found to be 1.28 : 1.00, a deviation of approximately 7% from that of healthy goats. In the case of goat No. 1[illegible], whose left lung was atrophied through phrenicectomy, the ratio between the right and left lung was found to be 1.52 : 1.00, a deviation of approximately 9% from that of healthy goat.

3. Thoracoplasty: When the left lungs of 3 goats were atrophied by thoracoplasty, the weight ratio between the left and right lung was 1.41 : 1.00, a deviation of 1.4% from that of healthy goats.

When this value of weight change of the atrophied lung is compared with the numerical results of zinc oxide deposition as shown in Table III, it can be concluded that the decrease in the weight of the atrophied lung, itself, is not the sole reason for the increase of the zinc oxide deposition ration in the atrophied lung. For instance, the deposition ratio of the atrophied lung increased by 20% in the case of pneumothorax, while the weight of the atrophied lung was scarcely decreased from that of healthy animal. In the case of phrenicectomy, the ratio of the zinc oxide deposition in the atrophied lung increased by 30%, while the weight of the atrophied lung was reduced only by 9%.

F. SUMMARIZATION AND DISCUSSION

In this experiment, it was confirmed through microscopic examination and quantitative analysis of zinc oxide that the settlement of inhaled foreign substances was very marked in the atrophied lung when compared with the normal lung and that the upper lobe contained a greater amount of dust deposition than the lower lobe. The reason for this is as follows:

1. In the case of pneumothorax, which equally and uniformly atrophied a lung towards the pulmonary hilus from every direction, it is natural that the upper lobes contain the largest amount of dust deposition if the animal is killed within a limited time after the last inhalation of foreign substance.

2. In the case of phrenicectomy, the ratio between the left and right lungs was absolutely inverse to the experiment reported in Part II, i.e. the lower lobe contained a larger amount of dust deposition than the upper lobe due to the effect of phrenicectomy. Thus, it may be deduced that unlike pneumothorax, phrenicectomy exerts uneven influence upon various regions of the treated lung with the lower lobe receiving the most pronounced influence. Comparison of the upper lobe of the atrophied lung with that of other normal lung revealed that the former contained a larger amount of dust deposition than the latter. Therefore, it may be said that although the upper lobe of the atrophied lung remains more active than its lower lobe, the respiratory motion or the atrophied lower lobe is somewhat impeded when compared with that of the healthy upper lobe.

In the case of thoracoplasty, the influence of the atrophy upon the settlement of inhaled dust particles was more similar to that of pneumothorax than to phrenicectomy.

G. CONCLUSION

The conclusion arrived at in this experiment was contrary to that of the former experiment in which a lung of the test animal was atrophied prior to the inhalation of foreign substances.

The inhaled microscopic foreign substances settled in the various regions in the same ratio as in the case of the healthy lung when pneumothorax was performed. In the case of phrenicectomy, the results were completely the opposite to that reported in Part II, i.e. the settlement of the inhaled dust particles was pronounce in the upper lobe and obscure in the lower lobe. The results of thoracoplasty was similar to that of pneumothorax.